DISEASES of the CHEST

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Air Pollution and Chest Disease*

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Since the beginning of the Industrial Revolution 200 years ago, man has been rather blithely belching ever increasing quantities of a staggering variety of noxious fumes into the surrounding atmosphere and then breathing the stuff every day. Until recently man's lack of concern was quite remarkable. True, it had been known for many centuries that smoke in quantities sufficient to suffocate, or that special kinds of poison fumes, could be lethal; and in the past century it was learned that industrial workers were sometimes endangered by in-plant exposure to the special industrial dusts and fumes. But it was always assumed that the great outdoor atmosphere was a limitless sea which could render harmless by dilution anything thrown into it, even in our prosperous smoking cities.

However, it is now known that when impurities in community air reach high enough levels, they do indeed cause disease and even death. The smog disasters of the Meuse Valley in Belgium in 1930; Donora, Pennsylvania, 1948; London, England, 1952, 1956, and 1957 have made this fact irrevocably clear. Although these episodes are well documented, there have undoubtedly been others which have passed undocumented and, perhaps, even unnoticed. The atmospheric scientists have now dispelled the illusion of the limitless sea of air; they have demonstrated that it has very definite boundaries and so is without the infinite cleansing and diluting powers which man had so long intuitively believed that it had.

Although it is now an established fact that these dramatic build-ups with their acute effects can occur and probably will occur with ever increasing frequency unless something is done, is this an all-or-none phenomenon? That is, when the undramatic, everyday levels of pollution prevail, does absolutely nothing harmful happen to those who constantly breathe it? From many indications, we who work full time in this field believe that these seemingly harmless, everyday levels of community air pollution do have cumulative, even though subtle, effects in chronic disease. But it little matters to the crippled and the dead whether it came about dramatically and obviously or slowly and without awareness. To secure ultimate answers on these undramatic, yet inexorable chronic effects is the challenge which must be met.

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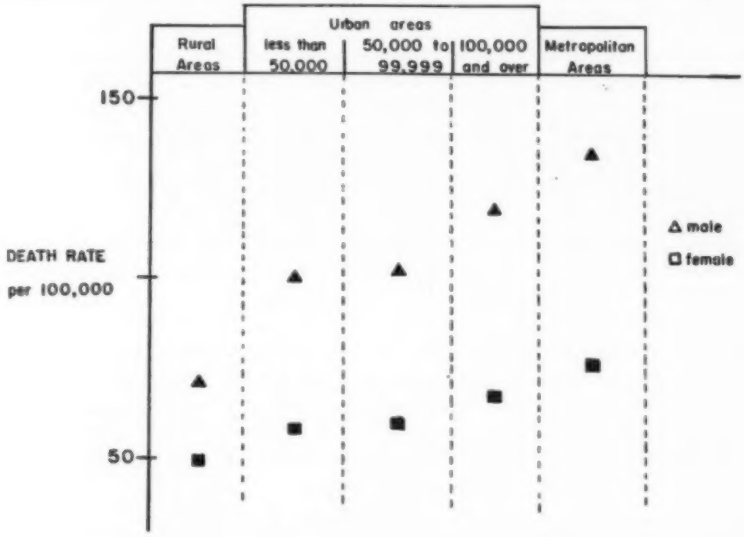
Is air pollution an important cause of chronic obstructive emphysema? Is there a significant counterpart here in the United States to the serious British "air polution disease," chronic bronchitis—or is it peculiarly a British problem? Is air pollution an important etiologic factor in our great increase in bronchogenic carcinoma? Do we have any variants of Yokohama or Okinawa asthma here in the United States? To what extent does air pollution aggravate pre-existing chronic pulmonary disease? In what other ways and to what extent does community air pollution affect human health?

These are the kinds of questions which must be answered so that intelligent recommendations for the costly remedies necessary to control community air pollution and also wise decisions in the handling of certain patients can be made. These challenging questions demand many new approaches and, unfortunately, require much time and money.

In response to an awareness of this need which was partly shocked into being by the Donora disaster of October, 1948, and partly brought about by the sober efforts of a few perceptive individuals, the United States Technical Conference on Air Pollution was called together in 1950 to bring the best available opinion together in one focus, so that the problem could be defined on a national level and future action better determined. Perhaps the most important result of this conference was passage of Public Law 159, which, in 1955, called into being the Air Pollution Program of the Public Health Service as a continuing focal point of national effort.

Even though a small professional staff was designated to explore the problem, the vast and diffuse nature of the work with its many ramifi-



BRONCHITIS Mortality by Population Density in ENGLAND and WALES, 1951.
(according to Pemberton and Goldberg)

FIGURE 1

cations in engineering, political, social, economic, and health areas requires a much larger and broader participation. Accordingly, the Surgeon General of the Public Health Service called the National Conference on Air Pollution in November 1958. Over 900 representatives from Federal, State, and local health units, industry, citizens' groups, clinical medicine, and a score of other professional disciplines, pooled their knowledge and provided guidelines for future action.

The conference successfully achieved its purpose—which was to take a national look at the meaning of air pollution—what is it? What does it do? And what should be done about it? But conferences do not solve problems. The two questions "what is it?" and "what does it do?" can only be answered by engineers, physical scientists, biologists, and physicians (both clinical and public health).

To the Air Pollution Medical Program is addressed the question "what does air pollution do—to man himself?"

By describing what we are thinking and doing in this new and rather perplexing but exciting work, this paper endeavors to sketch the problem and stimulate the interest of the non-Federal physician.

Some good work has already been done, and we know a great deal more than we did ten years ago. We now know something about the dramatic acute effects and probably how they are mediated. We are getting something better than mere guesses on aggravation of preexisting disease such as emphysema. We are getting more than a slight glimpse into the chronic bronchitis problem in Great Britain and the probable role of air pollution.

But we have just scratched the surface. We need to know more, much more. And this knowing isn't going to come easily.

How do we go about finding answers to these questions? One of the first things to do is to take a quick look at what is available; so we have examined the existing mortality and morbidity statistics. Even though there are many short-comings and necessary qualifications to this type of approach, we have obtained good information. For example, the more than 4,000 deaths caused by the London smog of December, 1952 were not even noticed until many months later when the vital statisticians were compiling their records. There are many examples of the type of leads furnished us by the statisticians. Figure 1 demonstrates a stepwise increase in chronic bronchitis mortality for both males and females in England and Wales as urbanization, and hence industrialization, increases. Figure 2 demonstrates a similar trend from emphysema mortality here in the United States. We are making every effort to improve the quality of the data reported and collected in the future—especially the morbidity data—while continuing this type of investigation.

Although statistical correlations do not prove a causal relationship, they can provide valuable clues for further investigation.

Of course, basic laboratory studies have also been instituted, observing the effects of artificial smog, using tissue culture techniques, disruption of cellular enzyme systems, disturbance of plant respiratory physiology, effects on bronchial ciliary activity of animals, skin painting and respiratory pellets for carcinogenesis, various studies on basic pulmonary

physiology, etc. But, as you know, this type of work requires time and the number of investigators so far involved is too small.

A standard toxicologic procedure is to substitute animals for people. Animals are more cooperative, and less costly to maintain; their natural life span is much shorter; their genetic make-up is more certain; their activities are far less variable; and they are much more amenable to environmental control.

However, even with the advantages of using animals these chronic exposure studies are costly and time-consuming. And, of course, what pertains to a strain C-57 black mouse must then be extrapolated to the human.

From examination of all available morbidity and mortality data here and in Britain, from knowledge gained from the famous acute smog episodes, from autopsies of exposed animals, from studies such as Motley's emphysema patients whose residual volume diminished after 20-40 hours in a room whose air supply was passed over activated charcoal filters, and from Amdur's work at Harvard demonstrating an increase in pulmonary resistance in guinea pigs following inhalation of sulfur dioxide, and from the common sense view that the organ system in closest contact with a noxious agent is at the greatest risk, it appears that the respiratory system is the prime target organ of inhaled air pollutants and that emphysema, chronic bronchitis, bronchogenic carcinoma, and possibly some forms of asthma are the disease most likely

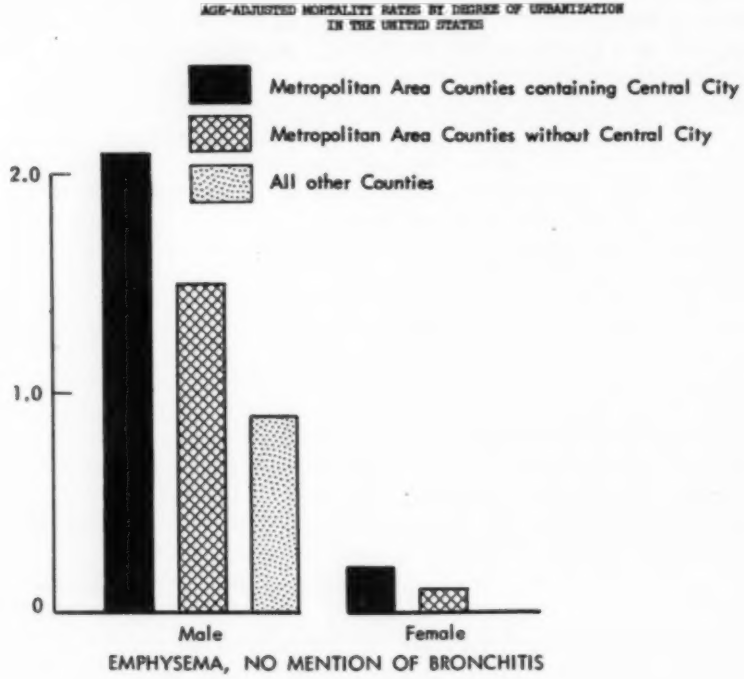


FIGURE 2

influenced by air pollution. Hence, our primary concern in pulmonary physiology and chest disease and the clinical chest physician's interest in the problem of air pollution.

There is only one type of experiment which would really answer these questions once and for all. Although it is only an ideal study model and completely impossible to carry out, it can illustrate the scope of the problem.

Take a sample of people, such that they are perfectly representative of our entire population. Then divide them into separate groups which will be large enough to give significant numbers of observations for every variable under study.

These groups must be perfectly matched against each other genetically and will live their entire lives under conditions which are identical in every respect save one—the air they breathe. One group will have perfectly clean filtered air, another the oxidant type smog of Los Angeles, another the reducing type smog of the soft-coal-burning cities of England and our eastern sea-board, and another will be high in industrial metal wastes, and so forth and so on, with all possible combinations thrown in. Naturally, the amount and types of smoking, and who smoked would be rigidly pre-determined in all groups. The only variable would be community air pollution. The subjects would be studied thoroughly throughout life—and probably for several generations—by perfect diagnostic teams with perfect instruments. Selected samples would be sacrificed along the way to gain additional information. And, of course, this whole study would be conducted under the "double blind" technique.

But man, being naturally perverse and uncooperative, and 70 years or more being a long time to wait, I am sure these ideal conditions can never obtain. We must then make compromises—usually great ones—bowing to the exigencies of reality and yet trying to somehow approximate this ideal model.

Our first big attempt to approximate this model—and our largest study yet undertaken—is a community health study in Nashville, Tennessee. This study is by no means perfect and is more in the nature of a pilot study.

One of the reasons Nashville was chosen is because its rather unique air pollution pattern allows an approach somewhat similar to that used in the laboratory where exposed and control groups can be well defined. Nashville is not excessively industrialized, so that for the six warm months of the year its residents enjoy a cleaner atmosphere than those of many other cities, but a great deal of soft coal is used for heating (both in homes and industries) so that for the other six months there is a heavy pall of sulphurous smelling smoke over much of the city. In addition this heating pattern is not uniform throughout the city so that distinct geographic areas can be differentiated within the city in respect to air pollution.

In cooperation, our Engineering Program has set up an elaborate network of 123 air sampling stations to measure the pollution both as it varies from day to day in the same place and as one area in the city differs from another.

Against this background of air sampling data a health survey is being conducted which consists of four parts. First, mortality data being collected will tell how many deaths, and of what type one area has against another. Next, degrees of pneumoconiosis are being determined on consecutive autopsies to be correlated with area and duration of residence. The third and fourth studies are at once more pertinent for illustration and more difficult.

The third study follows a selected panel of several hundred cases of known chronic chest disease, primarily asthma, and attempts to correlate daily variations in their clinical condition and pulmonary function to the measured air pollution levels.

By far the biggest, the fourth study is a city-wide morbidity survey in which trained teams using a carefully constructed questionnaire have interviewed some three thousand pre-selected families (which represents about ten thousand people) to enumerate the diseases which were present at the time of the interview and those which had occurred in the past. The amount and types of disease will subsequently be correlated with geographic area and with pollution levels existing at the time of interviews.

Of necessity, this Nashville Study deviated greatly from our hypothetic perfect study. Being our first venture of this sort, it must be regarded as a pilot study bound to raise more questions than answers but which, nonetheless, will refine our technique in the future. The Nashville Study was described here to show where our interests lie and where we are going and what areas need stressing. In this study we encountered several stumbling blocks which must be resolved before we can proceed with a more refined study.

We must identify all the people in a given population afflicted with the asthma-chronic bronchitis-emphysema disease spectrum and have some fairly accurate standardized way of measuring and describing the stage of progression of the disease. Unfortunately, most of our sign posts point towards these rather poorly defined and not too well understood disease entities which have an even more poorly defined symptom group of cough, wheezing, and shortness of breath.

We need to know much more about these diseases—their natural history and pathogenesis—to be able to define and detect them better and to standardize terminology. This is a big order, indeed, but it must be done.

We also must obtain objective measurements, counterparts to PPD and 70 millimeter film if you will. We would like this instrumentation not only to help identify for screening purposes but also, if possible, to quantify the amount of disability so that in two, three, or four years we could re-test the different groups and be able to say how much more one group's disease had progressed over the others. We would also like enough sensitivity to detect daily variations in pulmonary airway resistance, as was attempted in our panel study.

To be useful for mass screening the pulmonary function tests must have the necessary sensitivity and also be simple and palatable. The instrumentation should be reliable, and sturdy enough to be handled by field workers with a minimum of training. It must also be portable.

These two areas—more adequate understanding and definition of the diseases and more adequate pulmonary function instrumentation—are so crucial as to threaten us with serious delays in this, our most important type of study, until more progress is made.

Those who have had experience in tuberculosis field work know how difficult mass case finding can be even when relatively good tools are available. Until skin testing and mass x-ray became useful tools effective TB case finding was virtually non-existant. We are in this early stage now.

This has been a brief sketch of the air pollution problem today. With our phenomenal population and industrial growth, it will be an ever increasing problem in the future. I have tried to present a view of what we who are working full-time in the field of health effects of air pollution are doing and thinking so as to stimulate greater interest and wider participation in this air pollution problem which affects all of us, both as physicians and as breathing citizens.

SUMMARY

Acute smog disasters have made it clear that air pollution can cause disease and death. The subtle effects of everyday air pollution are, however, less well known, and present a formidable challenge to medical researchers.

Statistical correlations based on morbidity and mortality and laboratory studies, constitute the two main directions taken to determine long-term health effects. Neither approach yields results comparable to those which might be expected from long-term, well-controlled, prospective epidemiologic studies from which all variables except the air breathed would be eliminated.

A large-scale community health study in Nashville, Tennessee, by the Public Health Service represents the first venture in this field. Morbidity and mortality findings will be correlated with information from an elaborate air sampling network, while other environmental and cultural factors are standardized.

But studies much more elaborate than the Nashville study are needed. In the meantime, the need for refined portable pulmonary function instrumentation and for more accurate definition of the disease spectrum under question (asthma—chronic bronchitis—emphysema) are so crucial as to threaten serious delays.

RESUMEN

Los desastres agudos del "smog" han aclarado que la polución del aire puede causar la enfermedad y la muerte.

Los sutiles efectos de la polución atmosférica cotidiana, son siem embargo menos conocidos, y significan un formidable problema para los investigadores médicos.

Las correlaciones estadísticas basadas en la morbilidad y la mortalidad así como en los estudios de laboratorio, forman las dos sendas principales que han de seguirse para determinar los efectos a large plazo sobre la salud.

Ningún método rinde resultados comparables con los que pueden esperarse de los estudios a large plazo, bien controlados con base epidemiológica de los que se eliminen todas las variables exceptuando el aire respirado.

Un estudio en gran escala realizado en la comunidad de Nashville, Tennessee, por el Servicio de Salubridad Pública representa el primer intento en este terreno. La morbilidad y la mortalidad se correlacionarán con la información extraída de un sistema de muestreo del aire, en tanto que los otros elementos ambientales y culturales son uniformes.

Pero se necesitan estudios mucho mas complejos que el de Nashville.

Mientras tanto, la necesidad de instrumentos portátiles para valuar la función pulmonar y para la mejor definición del espectro de la enfermedad en cuestión (asma —bronquitis-crónica—enfisema) es tan importante, que el retardar esta investigación constituye un peligro.

RESUMÉ

Les catastrophes dues au brouillard ont montré de façon évidente que la pollution de l'air peut causer des maladies et la mort. Les effets inappréciables de la pollution de l'air que l'on respire chaque jour sont cependant moins bien connus et présentent un formidable champ d'action pour les chercheurs médicaux.

Des corrélations statistiques fondées sur la morbidité et la mortalité, et les études de laboratoire constituent les deux principales directions prises pour déterminer les effets à long terme sur la santé. Aucune de ces tentatives ne produit des résultats

comparables à ceux que l'on pourrait obtenir d'études épidémiologiques par prospection, à long terme et bien contrôlés, d'après lesquelles toutes les données variables seraient éliminées sauf l'air respiré.

Une étude de la santé publique pratiquée sur une large échelle à Nashville (Tennessee) par la Service de Santé Publique représente la première expérience dans ce domaine. Les constatations de morbidité et de mortalité seront confrontées aux renseignements donnés par un échantillonnage d'air tandis que les autres facteurs de milieu et de culture sont standardisés.

Mais des études beaucoup plus approfondies que celles de Nashville sont urgentes. En attendant, la nécessité d'une bonne instrumentation transportable pour l'étude de la fonction pulmonaire et pour une définition plus précise de l'aspect de la condition pathologique en question (asthme, bronchite chronique, emphysème) est si importante qu'elle ne peut souffrir des délais sérieux.

ZUSAMMENFASSUNG

Akute Unglücksfälle durch Nebel haben es augenfällig werden lassen, daß Verunreinigung der Luft zu Krankheit und Tod führen kann. Die heimtückischen Wirkungen der alltäglichen Luftverunreinigungen sind allerdings weniger bekannt und stellen für die ärztlichen Forscher eine beträchtliche Belastung dar.

Statistische Korrelationen, ausgehend von Morbidität und Mortalität und Laboratoriumsuntersuchungen, machen die beiden Hauptrichtungen aus, die man zur Bestimmung der Beeinflussung der Gesundheit auf lange Zeiträume eingeschlagen hat. Keiner dieser Wege führt zu Resultaten, vergleichbar denjenigen, die zu erwarten sind von sich über lange Zeiträume erstreckenden, wohl geprüften prospektiven epidemiologischen Untersuchungen, bei denen alle variablen Größen ausgeschlossen sind,-abgesehen von der Art der Atemluft.

Und eine Untersuchungsreihe in großem Maßstab eines Kommunalverbandes durch den öffentlichen Gesundheitsdienst in Nashville, Tennessee, stellt den ersten Einsatz auf diesem Gebiet dar. Ergebnisse hinsichtlich Morbidität und Mortalität werden in Beziehung gesetzt zu Informationen eines Netzes von hochentwickelten Luftsammelstationen, wobei andere kulturele und Umweltfaktoren genormt sind.

Es sind jedoch weit mehr ausgearbeitete Untersuchungen als bei der Nashville-Untersuchung erforderlich. Bis dahin ist der Bedarf nach verfeinerten tragbaren Lungenfunktionsgeräten und nach einer genaueren Definition des in Frage stehenden Krankheitsspektrums (Asthma—chronische Bronchitis—Emphysem) so entscheidend, daß ein ernsthafter Verzug droht.

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The Surgical Approach to Pulmonary Emphysema*,**

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To define pulmonary emphysema is difficult because it is a complex disease.[23,28] There is one type of pulmonary emphysema that results from an unknown cause (primary or idiopathic), and another type that is the result of a known disease previously involving the lungs (secondary type). In either condition the disease may involve the lungs generally or only in a localized area.

It is easier to understand and describe the disease if it is classified in the following manner:

1. Primary or idiopathic obstructive pulmonary emphysema
   (a) Generalized or diffuse bilateral involvement of the lungs (with or without a good heart).
      1. With blebs and/or bullae
      2. Without blebs and/or bullae
   (b) Localized area of lung involved[3] (subsegment, segment, lobe or one lung); the remainder of the lung without obstruction to air flow.
2. Secondary obstructive pulmonary emphysema
   (a) Generalized or diffuse bilateral involvement of the lungs.
      1. With blebs and/or bullae
      2. Without blebs and/or bullae
   (b) Localized area of lung involved (subsegment, segment, lobe or one lung); the remainder of the lung without obstruction to air flow.

This study is concerned with the primary idiopathic, obstructive bilateral pulmonary emphysema of the diffuse type, with and without blebs and/or bullae, and with or without a good heart. The other types of primary and secondary emphysema will be considered briefly in the discussion.

In primary idiopathic, obstructive bilateral pulmonary emphysema the disease diffusely involves the lungs. It is a generalized lung condition. There is no area of normal lung tissue; however, all areas of the lungs are not involved equally by the pathologic process. The periphery of the lobe is usually the area most frequently involved by the disease. The lung tissue with the greatest amount of pathologic destruction is functionless as respiratory tissue. The elasticity of the lung is definitely reduced. The alveolar walls thin out and degenerate. The alveoli enlarge and coalesce by a breakdown of the thinned-out degenerated walls.[30] The capillaries of the alveolar walls degenerate, disappear and reduce the extent of the capillary bed,[31] thus increasing resistance to blood flow and causing the development of pulmonary hypertension and finally cor pulmonale. The lung becomes voluminous and in the state of expiration

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is much greater in volume than the normal lung.[3,9,18] The thorax in the emphysematous patient becomes more or less fixed in a state of full inspiration and the diaphragm is flat or depressed. Air will enter more readily than it will leave the lungs, yet no organic obstruction to the bronchiolar alveolar passages can be found on pathologic study.

There is no cartilage in the normal bronchioles. There are not enough elastic fibers in the walls of the bronchioles to hold them open as a rubber tube is held open. The bronchioles in emphysema are grossly and microscopically not unlike those in the normal lung.[19] The bronchioles are collapsible tubes (Fig. 1) and will collapse unless held open by a physiologic mechanism. The normal physiologic mechanism (Fig. 2a) which holds open the bronchioles in health or disease is the elastic collapsible lung held in an expanded state by a closed pleural space situated within the rigid chest wall. The elasticity of the expanded lung tissue is transmitted to the pliable walls of the bronchioles, holding them open by a circumferential elastic pull. This is the physiologic process that normally causes the bronchioles to increase in diameter as the chest expands on inspiration and decrease in diameter as the chest contracts on expiration. The elastic circumferential pull holding open the bronchioles in the expanded lung is never lost in the normal lung.

Primary idiopathic obstructive pulmonary emphysema with its voluminous lung is similar to forcing an inelastic lung of 6,000 to 7,000 cc. volume into a pleural space of 5,000 cc. capacity (Fig. 3). The voluminous

FIGURE 1: The photomicrograph shows a typical bronchiole in a collapsed state. It is not held open by the physiologic principle of circumferential pull resulting from the elasticity of the normal expanded lung.

emphysematous lung has lost its elasticity to a greater or lesser degree. The circumferential pull holding open the bronchioles is greatly impaired (Fig. 2b). It may be lost completely on forced expiration. By holding the chest in a state of complete inspiration the patient is able to retain some of the physiologic mechanism of circumferential pull upon the bronchioles, thus partially holding open the bronchioles on forced expiration. This pull is lost to a great degree on expiration and accounts for a greater obstruction to air flow on expiration.

The bronchial arteries arising from the systemic arterial system supply the bronchial structures. The bronchial arterial blood, after passing through its capillary bed, is collected into bronchial veins that empty into the pulmonary circulation. Bronchial veins do not empty (drain) into the systemic venous system. This fact is supported by the inability to demonstrate bronchial veins emptying into the systemic veins in the anatomic laboratory or at the operating table, although sought for diligently for many years. It is supported by the need to decompress the left side of the heart when the heart is bypassed with the cardiopulmonary bypass apparatus. The emptying of bronchial veins evidently takes place on the pulmonary arterial side of the pulmonary capillary bed since venous mixing cannot be detected by pulmonary physiologists.

The physiology or function of the autonomic nervous system on the tracheobronchial system and lungs is not clearly understood.[28] It is believed that the autonomic nervous system has control of the bronchopulmonary musculature and thus asserts some control of bronchial diameter and/or spasm. The autonomic nervous system is thought to have some control of resistance to pulmonary blood flow through the pulmonary capillary bed and asserts an effect upon the character of secretions from bronchial glands and from mucous cells of the mucous membrane of the bronchioles. The function of the glomus pulmonale, with its sympathetic and parasympathetic nervous connections described by Krahl,[29] has not yet been clearly defined.

The operation for primary obstructive bilateral pulmonary emphysema with or without blebs and/or bullae, with or without a good heart, is directed at the reduction of lung volume by sacrificing lung tissue that is useless as a respiratory tissue. It is not directed at the removal of the pathologic conditions. In addition, the lung is denervated by a parasympathectomy and a local sympathectomy. The operation often is required on both sides of the chest and when necessary should be done at an interval of three or more months. The lung showing the greatest amount of disease is operated upon first.

Reduction in lung volume is brought about by resecting (Fig. 4 and 5) or plicating (Fig. 6) the areas of the lung most useless as respiratory

TABLE 1

		Postoperative Deaths		Late Deaths		Unimproved		Improved	
	Number	No.	per cent	No.	per cent	No.	per cent	No.	per cent
Total number patients operated	56	9	16	6	10	5	9	42	75
Unilateral Operation	42	9	21	3	7	3	7	30	71
Bilateral Operation	14	0		3	21	2	14	12	85

tissue. This tissue is generally found about the periphery of the lobe of the lung. The lung volume is reduced to fit the expiratory phase of the pleural cavity on full expiration. Thus, the improved physiologic mechanism or circumferential pull holding open the bronchioles is restored to some degree. It cannot be restored to normalcy since it is generally agreed that the emphysematous lung has lost its elasticity to a greater or lesser degree. In the reduction of lung volume only useless tissue should be plicated or resected; every effort should be made to preserve functioning lung tissue; therefore, segmental resection and/or lobectomy should never be performed. In the reduction of lung volume by removing useless lung tissue, if a space containing blebs or bullae is removed it is reasonable to believe that some less diseased area of the lung that has been collapsed may be allowed to function; the use of this formerly collapsed tissue is more likely if the bronchioles are thus held open to allow the passage of air. The reduction in lung volume brings about a higher diaphragm and permits better functioning. The thoracic cage, if still flexible, assumes a more nearly normal position.

The second part of the operation is denervation of the autonomic nervous system to the bronchioles and lungs (Fig. 6). The parasympathetic fibers are removed by resecting and ligating all branches of the vagus nerve from the superior aperture of the thorax to the inferior pulmonary vein; the recurrent laryngeal nerve is spared but its branches to the pulmonary artery and the cardiac plexus are resected carefully. A local sympathectomy is carried out by periarterial stripping of the pulmonary artery, peribronchial stripping of the main bronchus, and perivenous stripping of the two pulmonary veins. The pulmonary ligament is removed. The bronchial arteries which are usually normal or smaller in

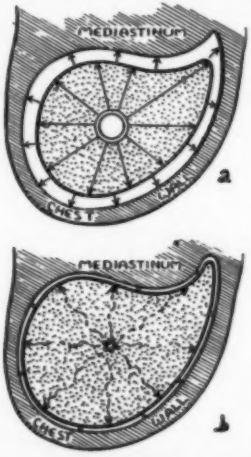

FIGURE 2: The drawing is an attempt to illustrate the effects of the physiologic principle of circumferential pull upon the bronchioles. This physiologic principle controls the size of the opening of the bronchioles. (a) The drawing indicates an elastic lung held expanded by a closed pleural space and a rigid chest wall. The elastic lung held expanded exerts its elastic pull upon the collapsible bronchioles in a circumferential manner, thus holding them open. (b) An illustration of the loss of the circumferential pull upon the bronchioles brought about by a large voluminous primary emphysematous lung during expiration. This is an important cause for expiratory airway obstruction in primary obstructive pulmonary emphysema.

size are resected in order to remove the sympathetic nerves they carry to the lung. The thoracic sympathetic trunk and the thoracic sympathetic ganglia are not disturbed. Thus, a localized sympathetic resection is accomplished. Until recently the glomus pulmonale was unknown but it is more than likely the glomus pulmonale has been denervated. Careful attention will be given to the glomus pulmonale in the future.

This report comprises an analysis of 89 patients with pulmonary emphysema studied primarily for the possibility of offering surgical therapy and brings up to date the series reported previously.[4-7] It is a consecutive series of private patients begun in 1950. The series includes only the primary or idiopathic bilateral obstructive pulmonary emphysema of the diffuse type with or without blebs and/or bullae, and with or without a good heart. The patients with localized pulmonary emphysema and secondary pulmonary emphysema have been omitted from this study since their problem is completely different.

A special study was rarely carried out when the series began in 1950. The occasional patient referred at that time had a desperate problem of dyspnea that had been clinically studied for months or years by a competent internist. The work-up of the dyspneic patient has gradually increased in scope and thoroughness. In approximately the past two years the study included adequate roentgenographic study with laminographs, fluoroscopy of the chest, bronchoscopy, bronchography, angiocardiography, right heart and pulmonary artery catheterization, kidney function, liver function and the pulmonary function studies that are available, namely, vital capacity, timed vital capacity, maximum breathing capacity, expiratory flow rate, various blood gas studies and blood pH. It is interesting to point out that even in the desperately dyspneic patient no untoward difficulty or complication has occurred as a result of these examinations. These studies have yielded valuable information but the results are difficult to correlate and summarize.

Of the 89 patients studied for operation only 56 (63 per cent) underwent operation. No patient was refused operation because he was suffering too great an impairment of respiratory function and no desperately dyspneic patient refused operation. Many were in a hopeless condition, being dyspneic at rest. Surgery was refused to 37 per cent because it was thought their disease was not far enough advanced to warrant it. Their symptoms were not sufficiently disabling or they had not received adequate medical treatment. A few patients were refused surgery because of coronary artery or left heart disease. Obviously, those who were dyspneic from causes other than primary bilateral pulmonary emphysema were rejected and not considered in this series. The following statistics were compiled from 56 patients who were operated upon. The youngest was 16, the oldest 73 years old; the average age was 58. There were 50 (90 per cent) men and 6 or 10 per cent women. There were 16 (30 per cent) with previous history of asthma. A family history of shortness of breath was noted in five (9 per cent).[35] The acute symptoms of dyspnea dated from a history of pneumonia in 20 (35 per cent). The average duration of symptoms before surgery was 70 months with a range from 12 to 192 months. There were nine (16 per cent) who died in the postoperative period. These deaths occurred after the first operation. Of the

group, 14 patients have had operation on both sides. There has been no postoperative death after the second operation. Six additional patients are expected to undergo the second operation. Only one side of the chest has been operated upon in 42 patients. Three (7 per cent) are not improved. One of the unimproved is included in the three (7 per cent) who have had late deaths. Thirty (71 per cent) of those who had unilateral operation are improved, Table 1. Of the 14 on whom bilateral operation has been performed, three (21 per cent) have had late deaths; two who had late deaths were not improved. Twelve (85 per cent) who had bilateral operation are improved, Table 1. In the group of 14 with bilateral operation none had blebs and/or bullae; three of these patients suffered right heart failure unless kept on a strict cardiac regime and these three are alive and improved.

The postoperative deaths can be accounted for as follows: two patients died in the early period of the study because of a technical error when lung volume was reduced to such an extent that the remaining lung could not fill the pleural space and air leaks could not be controlled.

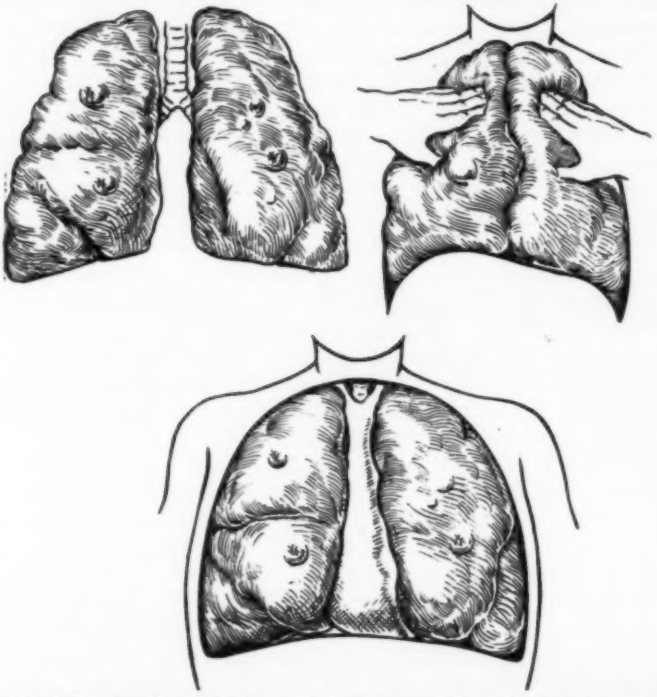

FIGURE 3: The drawings illustrate an important factor in primary generalized diffuse obstructive bilateral pulmonary emphysema with or without blebs and/or bullae. Whatever may be the primary causative factor in the development of emphysema in the late stages of the disease, expiratory airway obstruction caused by the loss of the physiologic principle of holding open bronchioles is an important factor. In the late stages of the disease it is very much like stuffing a diseased inelastic lung of 6,000 or 7,000 cc. capacity into a pleural space of perhaps 5,000 cc. capacity. It results in effects shown in Figure 2b. If lung volume is reduced by a surgical maneuver there will be a tendency to restore the results shown in Figure 2a. Restoration of the normal circumferential pull holding open the bronchioles can never be obtained since the elasticity of the emphysematous lung is lost to a greater or lesser extent.

Two deaths occurred because there was insufficient lung tissue to sustain the patients; yet no patient has been refused operation on the basis of severity of the disease. Two patients died on the hottest day of the summer in 1953. One of these probably died because of the heat, whereas the other was one of the two who had too little lung tissue to sustain him. One patient died of acute suppurative bronchitis; another of kidney failure or acute metabolic disturbance; one of left sided cardiac failure who obviously should not have been offered surgery. One patient, age 64, died from a cerebral lesion resulting in hemaplegia. There were six late deaths which occurred 4, 7, 12, 18, 26, and 48 months postoperatively. Three of these patients apparently received no real benefit from the operation, one being in the unilateral and two in the bilateral operation group. In the unilateral group there was one patient who showed no improvement and death occurred after four months. It is not known why he received no benefit from operation. In the bilateral group without improvement there were two late deaths, one of which resulted from coronary artery disease and left heart failure. Undoubtedly, this patient should have been refused operation because of his preoperative cardiac condition. The second late death in the bilateral group was the result of complications, primarily acute biliary tract and pyloric obstruction leading to inanition and death, there being too many complications for a patient with severe generalized pulmonary emphysema. In the other three late deaths the patients had shown satisfactory improvement that was sustained until death occurred. One of these died suddenly while traveling in Japan, another died suddenly while visiting a Virginia cavern, and the third died during sleep at night and the cause of death was not disclosed at autopsy.

The patient with generalized or diffuse secondary pulmonary emphysema is not a candidate for surgery. When one considers a patient who has had 25 to 50 per cent of his pulmonary capillary bed and alveolar areas destroyed by disease and then develops generalized emphysema, there is not enough lung tissue remaining to restore by surgery.

The patient with localized secondary pulmonary emphysema usually presents only the problem of the underlying lung disease. This is the type of pulmonary emphysema produced by Krahl[23] in the experimental animal. Ordinarily this type of emphysema is excised with the condition causing the obstructive area of emphysema. Often the area of emphysema attracts little or no attention. The remainder of the lung is normal and presents normal function.

In the patient with localized primary pulmonary emphysema the lungs are normal except for the area of pathology. There is no airway obstruction in the uninvolved lung tissue. It is difficult at times to distinguish between cysts of the lung and localized pulmonary emphysema. These localized areas are often merely space-occupying lesions without obvious symptoms and should be excised.[24,25] The authors have not treated unilateral pulmonary emphysema involving the whole lung except in infants. Excision of the lung is not the treatment of choice. Strictly unilateral[2,15] (one lung) primary obstructive emphysema in the adult, has not been observed, hence there is no comment on its treatment.

In selecting the patient for surgery some age limit should be established; however, a chronologic age cannot be set beyond which no operation is indicated. Generally, the younger the patient, the better the prognosis. The patient should have good kidney, liver and other glandular functions. The heart must be free of coronary artery and other disease, except cor pulmonale. Definite systemic hypertension is a contraindication. Right heart failure from pulmonary hypertension is not a contraindication; however, the patient cannot be operated upon until the cardiac failure has been corrected. Three patients of the bilateral

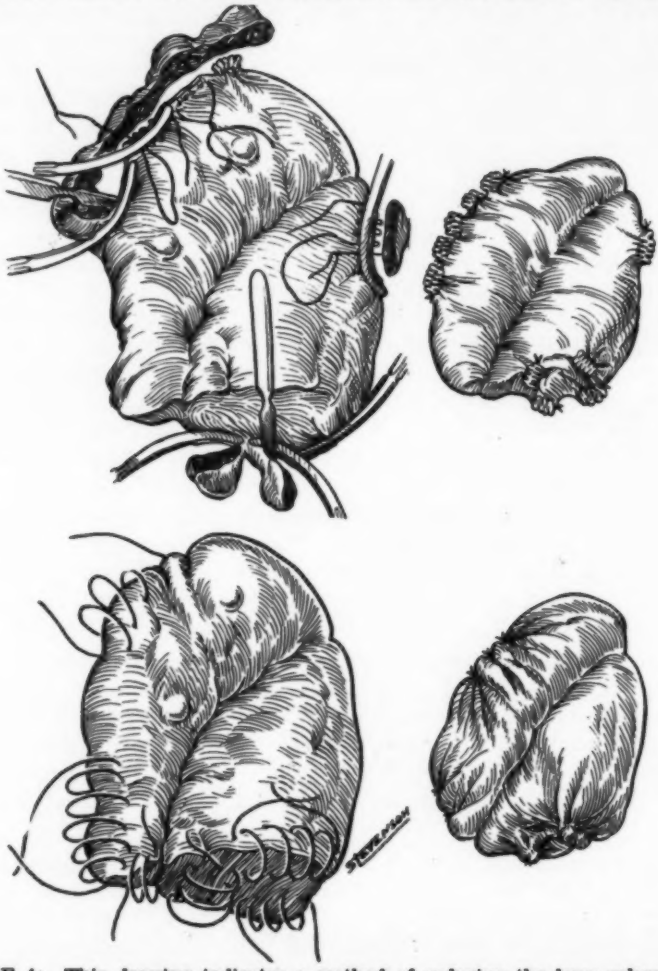

FIGURE 4: This drawing indicates a method of reducing the lung volume where there is primary generalized bilateral pulmonary emphysema without blebs and/or bullae. The volume of the lung is reduced by sacrificing the most functionally useless areas of the diseased lung tissue either by excision or by plication or by the application of both these methods. The puckering or pulling together by the suture reduces volume as great as the actual excision of lung tissue. Lobectomy and/or segmental resection should be avoided. The operation is directed at restoration of the physiologic principle of circumferential pull holding open the bronchioles and not at removal of pathology.

group were in continuous right heart failure before operation unless kept in bed. One, now five years after operation, is working and does not require digitalis. The other two have been free of cardiac failure since operation but are treated with digitalis.[16] There should be no other pulmonary disease unless the lesion is one that can be excised completely in the process of reduction in volume. This is a guarded statement since reasonably good capillary bed and functioning alveoli should not be sacrificed.

In considering the problem of primary generalized diffuse bilateral obstructive pulmonary emphysema and its treatment, either medically or surgically, it is clearly evident that lung tissue destroyed by disease cannot be restored. The patient may, however, be aided in utilizing the functioning lung tissue that he possesses, although the lung tissue is not entirely normal. Therefore, the result that can be obtained by treatment is directly related to the amount of functioning lung tissue that is possessed by the patient under consideration.

Primary pulmonary emphysema is by definition of unknown etiology; undoubtedly bronchial irritation, bronchial infection, and prolonged persistent cough contribute to its development.[23] Whatever the cause of the beginning of the disease, the loss to a greater or lesser degree of the physiologic principle of the elastic circumferential pull of the elastic lung holding open the bronchioles plays an important part in the well developed pulmonary emphysema. When the disease progresses to the stage where severe cough and/or forced respirations associated with considerable dyspnea occur, these expirations add to the obstructive factor as reported by Dayman[12-14] and others.[5,21] Obstruction to air flow becomes a part of a vicious cycle that causes worsening of the disease. The ideal time for treatment of the emphysema patient is in an early stage of the disease. The proper early treatment is medical and should be directed at the elimination of bronchial irritation and/or infection. There should be no smoking of cigarettes and the cough should be eliminated. When disease is more advanced it is evident that forced expiration caused by cough or physical exertion should be eliminated. Activity or work must be limited by the respiratory ability of the patient. Forced expiration only enhances the obstruction to outflow of air and causes progression of the disease. The judicious use of antibiotics, bronchial dilators, steroids, expectorants, breathing exercise, abdominal belts, and intermittent positive pressure breathing should be employed to their fullest extent in order that progression of the disease can be prevented. There is reason to believe that diligent treatment adequately followed by the patient for years may stop advancement of the disease. It is difficult in this or any other chronic disease to convince the patient of the need to continue treatment methods for the remainder of his life. Until the advanced stage of the disease develops the best treatment is medical care. However, judgment must be used since there is little or nothing to gain by medical treatment when the patient has progressed to the far advanced stage. When progression of the disease is inevitable, the primary obstructive pulmonary emphysema patient with or without blebs and/or bullae should be given the opportunity of surgery.[10,11,15-20,22,23,24,26] This should be done before the hopeless stage of the disease is reached.

There is often difficulty in understanding the difference in the pathologic physiology of patients with generalized diffuse primary bilateral obstructive pulmonary emphysema with blebs and/or bullae and those without blebs or bullae. Actually, both are variations of the same disease. There is generalized obstruction to the air flow throughout the bronchoalveolar system in both types. If this were not true, it would be localized emphysema. When there are blebs and bullae, usually there is a lesser degree of diseased lung in between these localized areas of more complete lung destruction. However, extensive blebs and/or bullae may indicate a greater degree of lung destruction. The removal of a large bleb or of a bulla from a patient with primary diffuse pulmonary emphysema

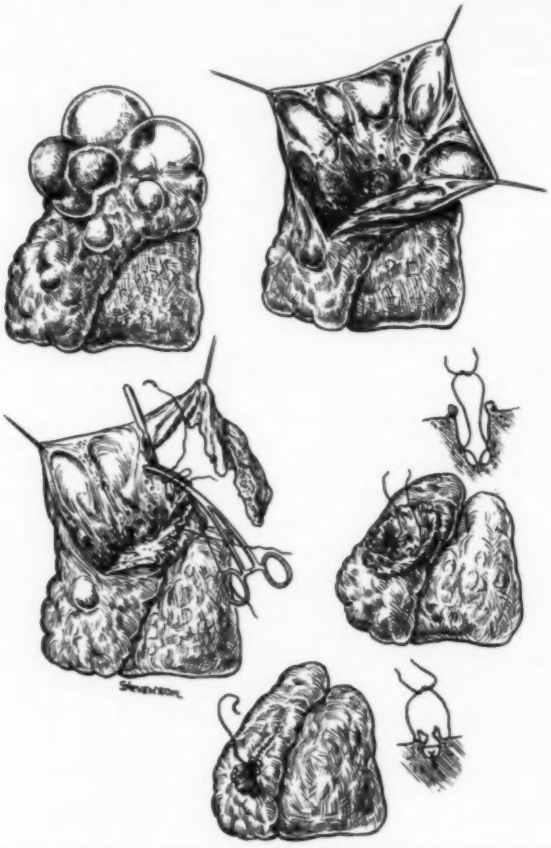

FIGURE 5: The drawing illustrates a method of reduction in lung volume in primary diffuse pulmonary emphysema associated with blebs and/or bullae. Lobectomy and/or segmental resection are avoided. The operation is directed at restoring the physiologic principle of circumferential pull holding open the bronchioles and not at removal of pathology. It should be remembered that the lung tissue in between the blebs and/or bullae are involved by the primary emphysema and have airway obstruction that is most marked on expiration. The emphysematous cyst-like area is incised. The functionally useless area around the periphery is excised by clamp and suture method. The internal walls or raw areas of the cyst-like structure are brought together by suture thus obliterating the cyst-like structure. Rarely is it necessary to individually suture a bronchiole or bronchus. A maximum of lung tissue is spared by this maneuver.

will not be the same as removal of a space-occupying lung cyst, since there is still the generalized obstruction to air flow through the bronchoalveolar system of the remaining lung tissue on both sides. The resection of a bleb and/or of a bulla reduces lung volume and improves respiratory function not only by allowing some adjacent lung tissue to expand and function, but respiratory function is improved by restoration of the physiologic principle holding open the bronchioles; thus, there is better air flow to and from all the remaining lung tissue. The understanding of the restoration of the physiologic principle of holding open the bronchioles permits the principle of reduction in lung volume to be applied to the emphysematous lung without blebs and/or bullae. Such a lung is reduced in volume by sacrificing functionally useless lung tissue through resection or plication. This procedure is not different than removal of a functionally useless bleb. In either type of lung the results obtained will depend upon the amount of lung tissue that can be brought into a position of function. There are rare cases in which the lobes on one side are unequally involved by disease. One lobe of the lung may occupy 75 per cent of the pleural volume. Reduction in size of the lobe will allow better use of the more nearly normal lobe and such a patient will experience great improvement in respiratory function. This obviously is true whether the large lobe occupied 75 per cent of the pleural space because of a large bleb or bulla or whether it was large because of diffuse emphysematous disease.

Lobectomy and segmental resection should not be employed since they often sacrifice unnecessarily the capillary bed and the alveolar membrane.[34] The operation should never be done to remove pathologic conditions. There are occasions in surgery when absolutely useless, functionless lung tissue should be allowed to remain because it will act as a filler of the pleural space. If there is too great a reduction in lung volume the air leaks will be uncontrollable and pleural pockets will encourage pleural complications. Improved respiratory function after operation depends upon avoidance of pleural complications.

In the opinion of the authors, denervation is an important factor in the operation and is carried out on all patients.[1,11,27,33,35] The patient experiences relief in partial or complete elimination of the troublesome morning cough and expectoration of a dram or two of tenaceous sputum. There is apparently no explanation of this relief except that denervation changes the character of secretions from the bronchial glands and mucous cells of the bronchiolar mucosa. Relief of this symptom alone generally is deeply appreciated by the patient. It is questionable whether bronchial spasm plays a part in true primary pulmonary emphysema; yet 30 per cent of the present series of patients had asthma before developing emphysema. Where there is some bronchial spasm it is relieved by operation and this undoubtedly is the result of denervation. Perhaps denervation reduces pulmonary vascular resistance.[18] Wescott[37] reports reduction in pulmonary artery pressure by use of oxygen.

It is interesting to speculate whether or not division of the bronchial arteries on both sides might reduce blood flow to the pulmonary capillary bed sufficiently to reflect beneficial effects on pulmonary vascular resistance. It may be possible that reduction in lung volume may also help in

some way to restore more nearly normal pressure in the thoracic vascular system and the remainder of the thorax. It is disturbing to speculate upon the ill effects of pulmonary infarction upon the lung in which the bronchial artery circulation has been destroyed. One patient in the series developed lobar pneumonia in the operated lung about 10 months after operation and tolerated the disease with no more difficulty than would be experienced by the patient with normal lungs.

Whether or not improvement is obtained by operation is evident, but it is not shown by pulmonary function studies used on these patients, except for a consistent increase in vital capacity.[16] Perhaps more delicate tests and tests more expertly carried out may produce different results. Improvement is shown by a feeling of wellbeing on the part of the patient. There is an increase in exercise tolerance. A diminution or loss of morning cough and a gain in weight are noted. There is a fall in elevated systemic blood pressure in six out of ten patients who showed hypertension before operation. Breath sounds are more audible and are in-

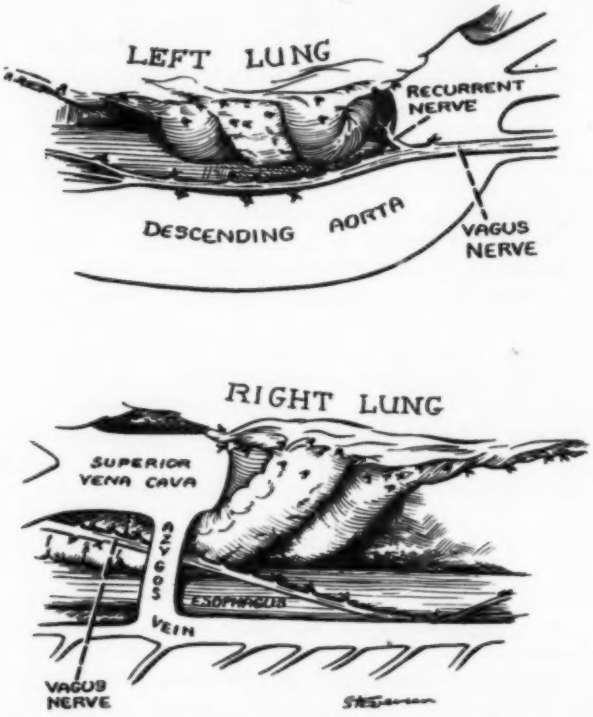

FIGURE 6: The drawings show the method of denervation of the lung. All branches of the vagus nerve are excised and ligated from the superior aperture of the thorax to the level of the inferior pulmonary vein. Of course, the recurrent laryngeal nerve is spared. However, its branches to the pulmonary artery and cardiac plexus are resected. The thoracic sympathetic ganglia and trunk are not disturbed. A localized sympathectomy is accomplished by means of periarterial stripping of the pulmonary artery, perivenous stripping of the two pulmonary veins, peribronchial stripping of the main bronchus, and resection of the bronchial arteries. The pulmonary ligament is divided. When the denervation is completed the lung is attached by the bare pulmonary artery, the bare bronchus, and the two bare pulmonary veins.

creased after cough instead of being decreased in the posttussic phase. Three of the surgically treated emphysematous patients have subsequently had other operations, one a cholecystectomy, two an inguinal herniorrhaphy; in these three patients there was no postoperative respiratory difficulty. When only one side is operated upon there is demonstrable shift of the mediastinum to the operated side on expiration, thus proving the function of the operated lung. Postoperative bronchography shows increased diameter of the smaller bronchi. The diaphragms are usually higher and move better than preoperatively. When the patients develop upper respiratory infection with or without bronchitis they respond to medical treatment more readily than before operation. They require minimal or no medication after operation and are freed from constant medical attention. In considering whether or not the patient receives improvement from operation one need only realize that the desperately dyspneic patient with pulmonary emphysema would not survive operation without this help. The patient tolerates the open chest operation for pulmonary emphysema with less trouble than he would an appendectomy.

There may appear to be a discrepancy in the discussion as to the desirability of bilateral operation since there are 30 patients alive and improved on whom only one side was operated. (In six of these, operation on the other side has been accepted.) These patients have received enough benefit from operation on one side to satisfy them. As an example, one patient, a partner in a small business, had not worked for five years. After the operation on one side he returned to his business and did not believe it fair to his partner to be away from work any longer.

Primary obstructive pulmonary emphysema is a relentlessly progressive disease without treatment.[20] Heretofore it was expected that progression of the disease would continue after surgery although relief was obtained. In spite of the experiences of other workers,[22,23] deterioration or progress of the disease has not occurred in the present series of patients. Surely, it must do so in time since this is a disease of aging. Progression probably has not occurred because relief of air way obstruction was obtained. Perhaps withholding of surgery until the far advanced stage of the disease was reached has allowed the ultimate in degeneration and further degeneration of the lung tissue is not possible even after relief is obtained by surgery.

When a patient with primary obstructive bilateral emphysema has had one lung operated upon successfully and later begins to lose the respiratory function gained by operation, it is the result of progression of disease in the unoperated lung.

If the loss of improvement after surgery is caused by the progression of disease in the unoperated lung, it will be revealed by roentgenographic study. Improvement in respiratory function will occur when this lung is treated by operation.

There has been no loss of respiratory function after operation or detectable increase of the disease in any patient who has had both lungs operated upon. The longest follow-up has been eight years. Undoubtedly, these patients will show progression of the disease some time in the future.

SUMMARY

Pulmonary emphysema is classified into primary and secondary types. Each of these is further subdivided into generalized and localized groups.

In the localized type of pulmonary emphysema there is airway obstruction only to the area involved by disease. The remainder of the lung is normal. In the generalized or diffuse type of bilateral pulmonary emphysema there is generalized bronchiolar-alveolar airway obstruction to all lung tissue whether or not there are blebs and/or bullae.

Bronchioles are collapsible tubes. They are normally held open by the physiologic principle of circumferential pull upon the bronchioles. The normal elastic lung is held expanded by a rigid chest wall which causes the lung elasticity to be transferred to a circumferential pull upon the bronchioles. As the chest expands on inspiration the bronchioles are enlarged. The relaxation of the chest on expiration causes the bronchioles to become smaller in diameter. Thus, the expiratory airway obstruction is at least partially accounted for in primary pulmonary emphysema.

Whatever may be the cause for the beginning of bronchiolar-alveolar airway obstruction in pulmonary emphysema, the partial loss of the physiologic principle of holding open the bronchioles is an important factor in the well developed disease.

Surgery directed at reducing lung volume by sacrifice of functionally useless pulmonary tissue can in some measure restore the partially lost physiologic principle of holding open the bronchioles.

Tenaceous sputum in small amounts is characteristic of pulmonary emphysema. The character of the secretion can be altered by denervation of the lung.

Of 56 patients operated upon for primary pulmonary emphysema, 42 (75 per cent) are improved.

When there occurs a loss of improvement gained by operation on one lung of a patient with primary pulmonary emphysema, the loss of function is usually the result of further degeneration of the unoperated lung. In none of the patients reported in this series has there been detectable evidence of further progression of the disease in the operated lung. The longest follow-up has been eight years. Undoubtedly, some patients will in the future show signs of further progression of the disease.

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RESUMEN

El enfisema pulmonar se clasifica en dos tipos: primario y secundario. Cada uno de éstos se subdivide en generalizado y localizado.

En el tipo localizado del enfisema pulmonar, hay obstrucción de las vías aéreas sólo en el área comprometida por la enfermedad. El resto del pulmón es normal. En la forma generalizada o difusa del enfisema bilateral hay generalización de la obstrucción de las vías aéreas y a todo el tejido pulmonar ya sea que existan o no ampollas o bulas.

Los bronquiolos son tubos colapsables. Permanecen abiertos normalmente por el principio fisiológico de la tracción circunferencial sobre los bronquiolos. El tejido pulmonar normal elástico se mantiene expandido por la pared rígida del tórax lo que hace que la elasticidad pulmonar se transfiera produciendo una tracción circunferencial sobre los bronquiolos. Cuando el tórax se expande en la inspiración los bronquiolos se ensanchan. El relajamiento del tórax en expiración hace que los bronquiolos disminuyan su diámetro. Así, la obstrucción expiratoria de las vías aéreas es por lo menos parcialmente responsable del enfisema pulmonar primario.

Cualquiera que sea la causa para el inicio de la obstrucción de las vías aéreas del enfisema pulmonar primario, la pérdida parcial del principio fisiológico que mantiene abiertos los alveolos es un factor importante en la enfermedad bien desarrollada.

La cirugía, orientada hacia la reducción del volumen del pulmón por el sacrificio del tejido pulmonar funcionalmente inútil, puede en cierta medida restaurar el principio fisiológico al que se debe el mantenimiento de los bronquiolos abiertos. El esputo adherente en pequeña cantidad es característico del enfisema pulmonar. El carácter de la secreción puede alterarse por la denervación del pulmón. De 56 enfermos operados por enfisema pulmonar primario, 42 (75 por ciento) han mejorado.

Cuando se observa que no hay mejoría por la operación, la pérdida de función es habitualmente el resultado de ulterior degeneración del lado no operado o a un desplazamiento franco del mediastino. En ninguno de los enfermos presentados en esta serie se ha podido descubrir prueba de ulterior evolución de la enfermedad en el lado operado.

El seguimiento mas largo ha sido de ocho años. Sin duda algunos de los enfermos mostrarán en el futuro evolución de la enfermedad.

RESUMÉ

L'emphysème pulmonaire se classe en deux catégories: primaire et secondaire. Chacune de ces catégories se subdivise ensuite en deux groupes: emphysème généralisé et emphysème localisé.

Dans l'emphysème pulmonaire de type localisé, il n'y a d'obstructio ndes voies respiratoires que dans la zone atteinte par l'affection. Le reste du poumon est normal. Dans le type généralisé ou diffus d'emphysème pulmonaire bilatéral, il y a une obstruction broncho-alvéolaire généralisée à tout le tissu pulmonaire, qu'il existe des bulles ou non.

Les bronchioles sont des conduits qui peuvent se collaber. Ils sont normalement maintenus ouverts par le principe physiologique de la pression circonférentielle sur les bronchioles. Le poumon élastique normal est maintenu en extension par une paroi thoracique rigide qui transmet l'élasticité pulmonaire sur la pression circonférentielle bronchiolaire. Comme le thorax se gonfle à l'inspiration, les bronchioles sont élargies. La mise au repos du thorax à l'expiration fait que les bronchioles deviennent plus petites en diamètre. En conséquence, l'obstruction du conduit expiratoire est au moins partiellement à mettre sur le compte d'un emphysème pulmonaire primaire.

Quelle que soit la cause du commencement de l'obstruction broncho-alvéolaire et vasculaire dans l'emphysème pulmonaire, la perte partielle du principe physiologique du maintien de l'auverture des bronchioles est un facteur important dans le développement de l'affection.

La chirurgie dirigée pour réduire le volume pulmonaire par le sacrifice de tissu pulmonaire fonctionnellement inutile peut dans une certaine mesure restaurer le principe physiologique partiellement perdu du maintien de l'ouverture des bronchioles.

Une expectoration tenace en petites quantités est caractéristique de l'emphysème pulmonaire. Le caractère de la sécrétion peut être altéré par l'énervation du poumon. Sur 56 malades opérés pour emphysème pulmonaire primaire, 42 (75%) son améliorés.

Quand survient une perte de l'amélioration obtenue par l'opération sur un seul poumon chez un malade atteint d'emphysème pulmonaire primaire, la perte fonctionnelle est généralement le résultat d'une dégénérescence ultérieure du poumon non opéré ou le résultat d'une atteinte médiastinale précise. Pour les malades appartenant au groupe étudié, on n'a pas pu mettre en évidence la preuve de la progression ultérieure de la maladie dans le poumon opéré. Le plus long contrôle a été 8 ans. Sans doute, certains malades à l'avenir montreront des signes d'évolution ultérieure de la maladie.

ZUSAMMENFASSUNG

Das Lungenemphysem wird in primäre und sekundäre Typen eingeteilt. Jeder Typ wird weiter unterteilt in generalisierte und lokalisierte Gruppen.

Bei den umschriebenen Formen des Lungenemphysems besteht eine Verlegung der Atemwege nur im Bereich des von einer Erkrankung betroffenen Gebietes. Die gesamte übrige Lunge ist normal. Bei den generalisierten oder diffusen Formen eines beiderseitigen Lungenemphysems liegt eine generalisierte Verengung der bronchoalveolären Luftwege des gesamten Lungengewebes vor unbeschadet dessen, ob kleinere oder größere bullae vorhanden sind oder nicht.

Die Bronchiolen sind leicht kollabierende Röhren. Sie werden normalerweise offen gehalten durch die physiologische Kraft des auf die Bronchiolen einwirkenden Zuges des umgebenden Gewebes. Die normale, elastische Lunge wird gespannt gehalten durch eine starre Brustwand, die die Ursache dafür ist, daß die Lungenelastizität auf einen Bronchiolen umgebenden Zug übertragen wird. In dem Maße, in dem sich der Brustkorb bei der Atmung ausdehnt, werden die Bronchiolen erwietert. Die Entspannung des Brustkorbes bei der Einatmung führt dazu, daß die Bronchiolen erweitert werden. Die Entspannung des Brustkorbes bei der Ausatmung bringt es mit sich, daß die Bronchiolen in ihrem Durchmesser kleiner werden. Es ist daher die expiratorische Verengung der Luftwege mindestens teilweise verantwortlich für ein primäres Lungenemphysem.

Wie auch immer die Ursache für den Beginn einer Verengung der bronchoalveolären Luftwege und Gefäßbahnen beschaffen sein mögen, ist es der partielle Verlust der physiologischen Fähigkeit des Offenhaltens der Bronchiolen, der ein wichtiger Faktor für die vollentwickelte Krankheit darstellt.

Ein auf die Verkleinerung des Lungenvolumens gerichtetes operatives Vorgehen mit Opferung funktionell wertlosen Lungengewebes vermag bis zu einem gewissen Grad, die z.T. verloren gegangene physiologische Fähigkeit, die Bronchiolen offen zu halten, wiederherzustellen.

Zähes Sputum in kleinen Mengen ist für das Lungenemphysem kennzeichnend. Der Charakter der Sekretion kann durch Denervation der Lunge beeinflußt werden.

Von 56 wegen primärem Lungenemphysem operierten Kranken wurden 42 (75%) gebessert.

Kommt es bei einem Kranken mit primärem Lungenemphysem, zu einer Wiederverschlechterung der Lunge bei einer operativ gewonnenen Besserung so ist der Funktionsverlust gewöhnlich die Folge einer weiteren Degeneration der nicht operierten Lunge oder auch die Folge einer definitiven Mediastinalverschiebung. Bei keinem der Kranken der hier wiedergegebenen Reihe fand sich ein nachweisbarer Anhalt eines weiteren Fortschreitens der Erkrankung in der operierten Lunge. Die längste Nachbeobachtungszeit betrug 8 Jahre. Zweifellos werden einige Kranke in Zukunft Zeichen eines weiteren Fortschreitens ihrer Erkrankung an den Tag legen.

Complete reference list will be published in the reprints.

Contribution of Bronchopleural Gas Leak, After Resection of Emphysematous Bullae, to CO_2 Excretion*

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Often, in the immediate postoperative period after resection of emphysematous bullae, the lung suture is not air-tight. The gas coming through the fistula so established is evacuated by the customary drainage tubes. When these patients, either during surgery or for a variable time postoperatively, are given artificial ventilation by positive pressure respirators, the gas leak occurs during inspiration.

As did many others, we thought that the leak was not contributory to alveolar ventilation, so that the amount of air lost through this channel should be subtracted from total inspired volume, in order to know the effective inspired volume. Expired volume should be measured otherwise and taken as the effective total ventilation, independent of the much larger inspired volume. We will show, however, that gas lost through this channel is, under these conditions, richer in CO_2 than expired air and contributes to alveolar ventilation in relation to its volume and CO_2 content.

Material and Methods

Persons with giant bullous emphysema are currently being studied in this Center and bullous resection is being performed in selected cases. In several patients, successive thoracotomies for bilateral bullae were done in the same operative session. Operative selection and results of treatment will be published elsewhere.

During surgery, ventilation was maintained with positive pressure and constant volume Engstrom respirator[1] applied by tracheal tube or tracheotomy. Anesthesia consisted of intravenous Pentothal and procaine. Blood gas and ventilatory measurements were conducted on some of the patients during surgery, according to the following methods. An indwelling Cournand needle was placed in the brachial artery. Expired gas was collected for three minutes in a Douglas bag placed in the expiratory side of the Engstrom apparatus. In the middle period of gas collection, arterial blood was sampled in heparinized syringes.

After bullous resection, while the patient was still anesthetized, the procedure was repeated, but the gas leaking through the pleural drainage tubes was also collected during several minutes in such a way that blood sampling occupied the middle minute of gas collections. Arterial blood CO_2 and O_2 concentrations were determined by the Van Slyke and Neill techniques, pH with a glass electrode and Beckman pH meter. Expired and pleural gas were analyzed for CO_2 by the Scholander gas

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analyzer. Arterial pCO_2 was estimated by Henderson-Hasselbach equation. Total ventilation was corrected for instrumental dead space. Volume of dead space was estimated by the Bohr equation.

In the second determination, the volume of gas collected through the drainage was added to expired volume to obtain total ventilation. CO_2 excretion included both expired CO_2 and that coming through bronchopleural fistula. By this procedure, alveolar ventilation and volume of dead space are influenced by the leak.

Results

Ventilatory and blood gas data are presented in Table 1. In the first case (J.B.), we were completely unaware of the possible influence of the gas leak. Due to some unexpected trouble, the first gas collection was started after one side had been operated on and was leaking already. Blood gas data were not forthcoming immediately, but after excision of the second bulla, expired volume was observed to drop almost in half, without changing the operation of the respirator. At the same time, the already present respiratory alkalosis was increased. Those facts induced considerable discussion, since it was quite apparent that arterial pCO_2 had dropped, in spite of a considerable reduction in expired volume. We decided to measure the volume and CO_2 content of the gas coming from the fistula and found out that it was quite considerable; unfortunately, expired gas was not collected simultaneously. The blood gas determinations showed that the respiratory alkalosis was being maintained. On

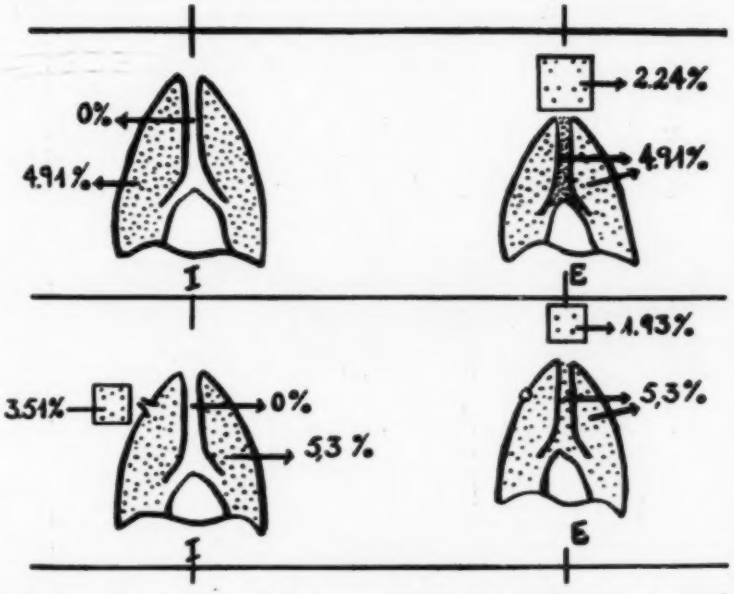

FIGURE 1: In the top part of the figure, the lungs are represented in spontaneous respiration. In the lower part of the figure, lungs under positive pressure respiration with a draining bronchopleural fistula. The figures represent CO_2 fraction and are those found in Case 2.

TABLE 1

Case	Name		Condition	Respiration	$\dot{V}_E$ 1/m.	F	V_T ml.	V_D ml.	$\dot{V}_A$ 1/m.	$\dot{V}_{CO_2}$ ml./m.	SaO_2 per cent	$CaCO_2$ vol. %	pH	$PaCO_2$ mm.Hg.	$F\,CO_2$ vol. %
1	J.B.		Preoperative	Spontaneous (air)	Tr. 9.570	25	383	244	3.210	173	85.8	52.9	7.39	48	2.44
		Operation	Right side operated	Positive Pressure ("Pure" O_2)	Tr. 9.690*	20	—	—	—	Tr. 129 P. —	100+.64	44.8	7.60	26	Tr. 1.55
			Both sides Operated		Tr. 5.230*	20	—	—	—	—	—	40.4	7.66	21	Tr. 0.80
			Closed Thorax		Tr. 4.440 P. 5.490 T. 9.930	20	Tr. 222 P. 274 496			Tr. — P. 142	100+.64	39.8	7.62	23	Tr. — P. 3.00
			Postoperative 2nd day	Positive Pressure ("Pure" O_2)	Tr. 7.566 P. 2.177 9.743	21	360 114 474	299	3.600	Tr. 118 P. 113 231	89.8	56.2	7.43	44	Tr. 1.86 P. 6.03
2	A.S.		Preoperative	Spontaneous (air)	Tr. 10.500	20	525	—	—	210	93.7	53.9	7.38	46	Tr. 2.43
		Operation	Closed Thorax	Positive Pressure ("Pure" O_2)	Tr. 7.000	20	350	180	3.385	137	100+.79	45.8	7.45	35	Tr. 2.24
			Both sides operated		Tr. 5.480 P. 1.910 7.390	20	274 95 369	198	3.430	93 58 151	100+.63	48.6	7.44	38	Tr. 1.93 P. 3.51
3	C.F.		Preoperative	Spontaneous (air)	Tr. 9.042	19	475	241	4.450	221	90.5	49.2	7.39	43	Tr. 2.58
		Operation	Closed Thorax	Positive Pressure ("Pure" O_2)	Tr. 8.150	22	370	241	2.840	138	100+.92	47.1	7.38	42	Tr. 1.80
			Both sides operated		Tr. 6.430 P. .969 T. 7.399	22	291 44 335	178	3.475	113 36 149	100+.68	45.0	7.42	37	Tr. 1.86 P. 3.96

V_E 1/m.: Expired volume 1/minute BTPS; F: Respiratory rate; V_T: Tidal volume; V_D: Dead space volume; V_A 1/m.: alveolar ventilation 1/min.; SaO_2: Arterial O_2 saturation; $CaCO_2$: arterial CO_2 content, volumes per cent; $PaCO_2$: Arterial CO_2 tension mm.Hg.; F_{CO_2}: per cent fraction of CO_2 in expired air or gas from pleural drains; Tr: Tracheal; P: Pleural drainage; T: Total.

*Gas lost through drainage tubes not measured.

the second postoperative day, still under positive pressure respiration by tracheotomy, the volume of CO_2 excreted through the fistula was similar to total expired (tracheal) CO_2.

Similar results were shown in Cases 2 and 3, though in this last one, CO_2 excreted through the drainage tubes was less important.

Discussion

The results shown demonstrate that the inspiratory gas leak through the fistula in these patients may be an important contribution to CO_2 excretion and therefore, to alveolar ventilation. It is probable that the respiratory alkalosis present in the first determinations in Case 1, when the right hemithorax already was closed, was due to the attempt by the anesthetist to maintain the same expired volume in spite of the gas leak through the fistula.

Although we have not devised a method to prove the mechanism of CO_2 excretion through the fistula, we believe that the following hypothesis may be advanced to explain the observed facts (Fig. 1). Bronchopleural fistula is most probably a site of decreased resistance in the airway, so that gas inspired under positive pressure may tend to flow through it preferentially with respect to time, that is, that the time-constant may be less than that of other normal pulmonary areas. At the end of expiration, anatomic dead-space is filled with alveolar expired gas. During the next inspiration, fresh air, free of CO_2, dilutes this alveolar gas so that the alveoli are finally ventilated by a mixture of air and the alveolar gas of the conducting airways. The resultant alveolar inspired gas contains a varying proportion of CO_2.

In our cases, we believe that the first portion of inspired gas goes along the lesser resistance pathway (*i.e.*, the bronchopleural fistula) washing out part of the alveolar gas placed in the conducting airways. Thus, the alveolar inspired CO_2 may be nearer to ambient air, while the CO_2 concentration of the fistula gas, collected during inspiration may be accounted for. These facts have some bearing in patients placed in the same situation, since, if we strive to keep their predicted expired volume, we will surely produce respiratory alkalosis according to the extent of CO_2 excretion through the fistula.

If CO_2 concentration in fistula gas is lower than alveolar (arterial) $\dot{C}O_2$ (Cases 2 and 3) it may be assumed that part of inspired gas (free of CO_2) is coming through the fistula. This portion of inspired gas would be wasted and, by application of Bohr equation, included in dead space volume. Whether dead space would be finally increased or decreased depends on the presence of other factors which might improve ventilation-perfusion relationships. In Case 3, the establishment of the fistula results in the reduction of physiological dead space volume. Since total ventilation decreased very little, respiratory rate did not change and CO_2 excretion increased, this may be taken as an index of better distribution of inspired gas, perhaps induced by the conditions referred to.

Based on these data, we may imagine the high CO_2 content found by direct puncture of some large bullae or air cysts might sometimes be an example of a similar fact if their bronchi could be considered as a lesser resistance path.

SUMMARY

Patients with large emphysematous bullae were subjected to surgical resection while breathing was maintained by a positive pressure, constant volume respirator. In some of them expired volume was seen to drop markedly when inspiratory gas leak through the sutures of bullae developed. Gas coming through that fistula was found to be rich in CO_2, thus contributing to alveolar ventilation. We believe that alveolar expired air, remaining in the conducting airway, and pushed through a lesser resistance pathway may be the source of CO_2 found in the collected gas leak. This fact should not be neglected when ventilation is artificially regulated in these patients.

RESUMEN

Se sometieron enfermos con grandes bulas enfisematosas a tratamiento quirúrgico mientras respiraban a presión positiva con el respirador a volumen constante. En algunos de ellos el volumen espirado se vió que caía marcadamente cuando había fuga de gas a través de las suturas de las bulas. El gas que escapaba a través de las fístulas se encontró rico en CO_2, contribuyendo así a la ventilación alveolar. Creemos que el aire alveolar expirado permaneciendo en las vías aéreas, y empujado hacia la vía de menor resistencia puede ser la fuente de 1 CO_2 encontrado en el gas de la fistula. Este hecho no debe desdeñarse cuando se regula la ventilación artificialmente fistula.

RESUMÉ

Des malades atteints de bulles emphysémateuses volumineuses subirent une résection chirurgicale, tandis que la respiration était maintenue sous pression positive, par un respirateur à volume constant. Chez certains d'entre eux, on nota que le volume

expiré tombait d'une façon nette lorsque se constitue une fuite du gaz inspiré à travers les sutures bulleuses. Le gaz venant à cette fuite se montre riche en gaz carbonique, contribuant par là à la ventilation alvéolaire. L'auteur pense que l'air alvéolaire expiré, restant dans le conduit aérien, et poussé à travers une zone de moindre résistance peut être la source du gaz carbonique trouvé dans la fuite du gaz collecté. Ce fait ne devrait pas être négligé lorsque la ventilation est réglée artificiellement chez ces malades.

ZUSAMMENFASSUNG

Bei Kranken mit großen Emphysemblasen wurde eine Resektion vorgenommen unter Aufrechterhaltung der Atmung mit einem Respirator mit positivem Druck und konstantem Volumen. In einigen Fällen war zu erkennen, daß die Expirationsluft merklich abfiel, wenn sich eine Undichtigkeit an der Naht der Blase bei der Inspiration entwickelte. Das durch diese Fistel einströmende Gas erwies sich reich an CO_2 und belieferte auf diese Weise einen Beitrag zur alveolären Ventilation. Wir glauben, daß die aus den Alveolen ausgeatmete Luft, wenn sie in den zuführenden Luftwegen verbleibt, und auf einen Weg geringeren Widerstandes geführt wird, vielleicht die Quelle der CO_2 ist, die sich in der luftdurchlässigen Stelle findet. Diese Tatsache sollte nicht vernachlässigt werden, wenn bei diesen Kranken die Atmung künstlich gesteuert wird.

REFERENCE

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THE RELATIONSHIP OF THE SYMPATHO-ADRENAL SYSTEM TO POTASSIUM FLUX AND CARDIAC IRRITABILITY INDUCED BY ALTERATIONS IN BLOOD pH

During respiratory acidosis, there is a rise in the potassium levels in both arterial and coronary sinus blood. Experiments carried out on groups of healthy dogs revealed interesting and important findings. In the immediate posthypercapnic period, there is a further rapid rise in these levels, that of the coronary sinus being much higher which indicates loss of myocardial potassium. This period of significant arteriovenous difference has a temporal relationship to severe cardiac arrhythmias.

Plasma levels of epinephrine and norepinephrine are elevated during respiratory acidosis. The posthypercapnic period is associated with a precipitous drop in the previously high levels. This too has a temporal relationship to the arrhythmias occurring at this time.

The administration of epinephrine or norepinephrine in the posthypercapnic period eliminates the negative arteriovenous difference in levels of potassium and prevents the occurrence of ventricular fibrillation.

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RUPTURE OF THE HEART FOLLOWING MYOCARDIAL INFARCTION

Cases of cardiac rupture secondary to myocardial infarction at the National Institute of Cardiology of Mexico were reviewed, as well as those published in the literature, with a physiopathologic and anatomic-electrocardiographic correlation. Twelve per cent of patients with recent myocardial infarction had cardiac rupture. Fifteen per cent of the patients dying within three weeks from the date of onset of infarction had cardiac rupture.

Cardiac rupture was more frequent among the elderly, among women, among patients with hypertension and among patients who did not stay at rest or who undertook physical effort during the course of myocardial infarction.

The electrocardiographic evidence points to myocardial rupture in patients with large areas of infarction; however, in numerous cases of infarction with rupture, the ECG showed only signs of small areas of necrosis. The depth of the area of infarction in the free wall of the left ventricle cannot be established electrocardiographically in some cases. The majority of authors admit that the incidence of rupture is greater among patients treated with anticoagulants.

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Pregnancy and Tuberculosis

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Prior to the chemotherapeutic era in the treatment of tuberculosis the voluminous available data presented conflicting views on the effect of pregnancy on this disease. The declining volume of literature published on the subject since the advent of chemotherapy probably reflects the current attitude among physicians that pregnancy in tuberculosis no longer poses a significant problem. That this opinion may be wrong, and that the subject may still be in need of serious study is indicated by the reported presence of tuberculosis in 1.5 to 2 per cent of pregnant women treated in the New York Lying In Hospital.[1] Similarly, Dorfman *et al.*[2] reported an incidence of 3.4 per cent of tuberculosis in their study. Since the introduction of chemotherapy very few controlled studies of this problem have been reported, and only a few of those reported have included a prolonged follow-up of the patients.

The present study was undertaken for the purpose of comparing a series of patients in whom pregnancy and active tuberculosis coexisted, and who were followed for a prolonged period of time, with a similar number of non-pregnant women with active tuberculosis, to determine whether or not pregnancy has any untoward effect on women whose tuberculosis has been treated, by present standards, with adequate chemotherapy.

Material and Methods

In this retrospective study are included all the women admitted to Lowman Pavilion, Tuberculosis Unit of Cleveland Metropolitan General Hospital with active tuberculosis and pregnancy from January, 1954 to December, 1958. The total number of patients was 53, in whom there were 64 pregnancies. The control group consisted of 53 women of similar age who were non-pregnant and who were in the hospital at the same time.

Age, Race and Background Data

The majority of the patients in both groups were between the ages of 20 and 35 years. There was preponderence of Negro patients in both groups. Both groups were well matched according to age, but there was

TABLE 1—COMPARISON ACCORDING TO AGE AND RACE

Age Periods:	Pregnant	Non-Pregnant
15 to 19 years	5	8
20 to 25 years	20	19
26 to 29 years	12	11
30 to 35 years	13	13
Over 35	3	2
Race:		
Negro	30	33
White	23	20
Total	53	53

TABLE 2—DIAGNOSIS AND EXTENT OF DISEASE AT THE TIME OF ADMISSION

	Pregnant	Non-Pregnant
Minimal	23	17
Moderately Advanced	16	20
Far Advanced	7	10
Miliary Tuberculosis	2	1
Tuberculosis of the Lymph Nodes	1	3
Tubercular Meningitis	1	0
Tuberculosis of the Spine	1	0
Pleural Effusions	2	2

a slight preponderence of Negro patients in the non-pregnant group (Table 1).

In the pregnant group the presence of tuberculosis was known before pregnancy in 20 patients, while in 33 the diagnosis was first made during pregnancy. During the period of observation 64 pregnancies were recorded in this group. One patient had three, nine had two each and 43 had a single pregnancy. Except for one miscarriage all of the pregnancies were delivered normally.

Sputum Status on Admission

In 35 (62 per cent) of the pregnant group and in 42 (79 per cent) of the non-pregnant group one or more positive sputum or gastric cultures were obtained at the time of admission. In the remainder repeated sputum and gastric cultures were negative for tubercle bacilli.

Diagnosis at the Time of Admission

Five cases in each group had only extra-pulmonary tuberculosis, while the remaining 48 all had pulmonary disease. As far as extent of disease was concerned the groups were almost completely comparable. There was a slight preponderance of cases with minimal disease in the pregnant group and of far advanced cases (Table 2) in the non-pregnant group.

Presence and Size of Cavities

Seventeen (32 per cent) of the pregnant and 19 (36 per cent) in the control group had a single cavity on admission while one in the former and three in the latter group had multiple cavities.

Treatment

Thirty-nine (74 per cent) of patients in the pregnancy group and 44 (83 per cent) in the control group received chemotherapy for the first

TABLE 3—NUMBER AND SIZE OF CAVITIES AT THE TIME OF ADMISSION

	Pregnant	Non-Pregnant
Total No. of Patients with Cavities	18	22
Single cavity	17	19
Multiple cavities	1	3
Cavity size less than 2 cm.	5	3
Cavity size 2 to 4 cms.	7	12
Cavity size over 4 cms.	5	7

TABLE 4—CHEMOTHERAPY AND PNEUMOPERITONEUM RECEIVED

Drug Regimens	Pregnant	Non-Pregnant
Isoniazid and PAS	23	27
Streptomycin and PAS	14	13
INH, PAS and Streptomycin	16	13
Other drugs in addition (PZA, Viomycin and Cycloserine)	2	3
Pneumoperitoneum with Phrenic Crush, in addition to drugs	6	7

time, while the remainder had previously received some form of chemotherapy. Twenty-three (43 per cent) cases in the first group and 27 (51 per cent) in the second group received INH and PAS; the others were on different regimens (Table 4).

The total length of treatment varied, but most of the patients were treated for 18 months or longer. In seven of the pregnant group and four of the non-pregnant group the patients were lost to follow-up after treatment periods of less than one year. Table 5 shows the total length of treatment for all patients. Thirty-nine (74 per cent) in the pregnant group and 40 (76 per cent) in the control group were kept on drugs for 18 months or more, before this therapy was discontinued as adequate.

Hospitalization

The total period of hospitalization varied. Approximately two-thirds of the patients in each group received a minimum of six months of hospital treatment. The others were discharged against medical advice after shorter periods of treatment (Table 6).

Total Length of Follow-up

After discharge from the hospital they were followed by the County Clinic where their drugs were continued until it was felt that the treatment had been adequate. Even after discontinuation of drugs they were followed by serial chest x-ray films at varying intervals depending on the extent of the residual disease, etc. For details see Table 7.

Results of the Study

The groups were compared as to sputum conversion, attainment of the stability of the disease as shown by serial roentgenography, rate and time of cavity closure, further need of surgery and rate of early and late relapse.

Sputum Conversion

Prompt conversion of sputum was noticed in 25 (72 per cent) of the positive pregnant patients and in 32 (76 per cent) of the control cases.

TABLE 5—TOTAL DURATION OF TREATMENT

Duration	Pregnant	Non-Pregnant
Less than 6 months	4	3
6 months to 9 months	3	1
1 year to 1½ years	7	9
1½ years to 2 years	21	30
Over 2 years	18	10

TABLE 6—TOTAL PERIOD OF HOSPITALIZATION

	Pregnant	Non-Pregnant
Less than 2 to 3 months (Left A.M.A. Not readmitted subsequently)	12	11
4 to 6 months	3	7
6 to 9 months	30	27
9 months to 1 year	6	4
Over 1 year	2	4

In all of these patients at least three sputa or gastric cultures were subsequently negative for acid-fast bacilli. Three in each group were still known to be positive at the time of the latest available follow-up.

Roentgenographic Follow-up

Forty-nine (92 per cent) of the cases in the pregnant group and 47 (89 per cent) of those in the control group showed improvement and stability of the disease by serial films. Three in the pregnancy group as compared to four in the control group showed some worsening of the disease under this observation period. Two in the control group did not show any change, while in one in the pregnancy group the changes were questionable and no adequate follow-up was available.

Cavity Closure and Need for Surgical Treatment

The indications for surgical resection were persistent cavity or, in a few cases, extensive residual disease.

The early result of treatment was that 49 in the pregnancy group and 47 in the control group achieved improvement and apparent stability of their disease while three in the first and four in the second group showed worsening. One of the former and two of the latter showed no change.

Results of Late Follow-up

Four (7.5 per cent) in the pregnancy group and six (11 per cent) in the control group had subsequent relapse of their disease occurring one or two years after their discharge. Of these, three in the first group achieved stability of their disease by subsequent admission and change in chemotherapy, while one is still open and positive. Similarly four in the control group achieved stability, while one died with far-advanced disease and one is still open and positive.

Discussion and Comments

Since the time of Hippocrates, when pregnancy was thought to be beneficial for phthisis to the opposite concept in the 19th century when the often quoted dictum was "For the virgin no marriage, for the married no pregnancy, for the pregnant no

TABLE 7—LENGTH OF FOLLOW-UP AFTER DISCHARGE FROM THE HOSPITAL

Duration	Pregnant	Non-Pregnant
No Follow-up	8	4
Less than 6 months	1	1
6 months to 1 year	6	5
1 year to 2 years	10	15
2 years to 4 years	10	21
4 years or more	18	7

TABLE 8—RATE OF SPUTUM CONVERSION FROM POSITIVE TO NEGATIVE FOR TUBERCLE BACILLI

	Pregnant	Non-Pregnant
Total No. of Patients Positive on Admission	35	42
Converted immediately	25	32
Converted within 3 to 4 months	3	2
Converted within 4 to 6 months	3	1
Converted after Surgical Resection	1	4
Not converted still Positive	3	3

confinement and for the mother no suckling," came the 1950's era when a more or less neutral position on this subject became popular.

Hedvall[2] in 1953 summed up very aptly and comprehensively the problem of pregnancy and tuberculosis. In his article he reviewed both pro and con views of this problem including the problem of therapeutic abortions up to that time. In his own series of 250 patients he did not observe any significant effect of pregnancy, either favorable or unfavorable, on tuberculosis. It is of interest to note that this change in the attitude among physicians occurred even before adequate chemotherapy for tuberculosis became well established.

Since Hedvall's article in the review of this subject in the English literature, Stewart and Simmonds[4] in a study of tuberculosis reports from England reported that the five year survival rate had no relationship to pregnancy.

However, Cromie[5] reported that in 101 cases of pregnancy and tuberculosis 20 of 30 relapses occurred in the first post-partum year. He further concluded from his study that half the cases with active tuberculosis will suffer an extension of their disease, while one-quarter of inactive cases will become reactivated and the crucial time for this is in the first three months of pregnancy or puerperium. But this study was done before adequate chemotherapy for tuberculosis was available.

That therapeutic abortions had nothing to offer in the treatment of pregnancy and tuberculosis was shown by Schaefer *et al.* in two published papers.[6,7] In the clinical management of pregnant tuberculosis patients, Schaefer[8] reported that twice as many women in whom tuberculosis was first discovered during pregnancy died of the disease as did in the group whose tuberculosis was known before the onset of the pregnancy. He also stressed the importance of prenatal chest radiographs in the early diagnosis of tuberculosis.

Pugh[9] also showed that the survival rate was higher among the patients in whom pregnancy occurred after they were already known to have tuberculosis, while mortality was higher among the patients in whom tuberculosis was diagnosed either late in pregnancy or in the puerperium.

Raeburn and Clancy[10] reviewed 41 pregnant hospitalized patients with active tuberculosis. All improved while awaiting confinement and in the puerperium and all received chemotherapy only in the puerperium.

Schaefer, Birnbaum and Douglas[1] reported 255 patients from 1952 to 1956 in whom 298 deliveries occurred. In three months post-partum follow-up they found 85.9 per cent improved, 10.4 per cent remained unchanged while only 3.7 per cent progressed. Bowerman[11] also did not find any deleterious effect of pregnancy on tuberculosis in his 92 patients. Dorfman *et al.*[3] similarly in their study of 162 patients with pregnancy and tuberculosis, both active and inactive, did not report any harmful effect of pregnancy. It was interesting to note that they also treated 98 of their inactive tuberculosis cases with prophylactic isoniazid during pregnancy; reactivation occurred

TABLE 9—RATE OF CAVITY CLOSURE AND NEED OF SURGICAL INTERVENTION

	Pregnant	Non-Pregnant
Total No. of Patients with cavities on admission	18	22
Closed within 3 to 4 months	6	7
Closed within 4 to 6 months	3	2
Cavities resected	5	8
Cavity still present with positive sputum	3	3
Open-Negative Cavity	1	2
Surgical Interventions:		
Lobectomies	4	9
Segmental Resections	1	0
Pneumonectomy	1 (Prior to pregnancy)	1

only in one of these patients. Selikoff[12] in conjunction with the same authors stressed that the prophylactic use of isoniazid in pregnant patients with inactive tuberculosis might prevent reactivation of their disease during pregnancy.

Flanagan and Hansler[13] also recently reported 22 patients with pregnancy and tuberculosis in comparison with a matched group of non-pregnant patients, treated with chemotherapy and hospitalized for six months. They did not observe any difference between the two groups regarding sputum conversion, cavity closure and radiological stability.

The Joint Tuberculosis Council report was summarized in *The British Medical Journal*[14] by the statement "It states firmly that pregnancy has no deleterious effect on tuberculosis; to which might be added the proviso that the infection receive effective treatment."

Lane,[15] reporting one to three year's follow-up of patients with pulmonary tuberculosis and pregnancy also did not find any deleterious effect of pregnancy on tuberculosis. He further questioned the idea that the patients should wait for two years after their disease became arrested to become pregnant. In his group there were 28 cases who became pregnant before the two year period had elapsed and there was reactivation of disease in only one case.

In *The Lancet*[16] in an article on "Obstetric Care of Tuberculosis Patients" it was reported that one case in 200 attending ante-natal clinics had active tuberculosis, and it further stated that 30,000 patients are delivered in the United States every year.

Ante-natal radiographs of the chest were recommended to be taken between the 13th and 26th weeks to avoid somatic damage to the fetus.

Regarding surgery in pregnancy with tuberculosis, William[17] reported 16 patients who had successful full term deliveries after surgical operations for their disease. Corner and Nesbitt[18] reported 47 collected cases of full term normal delivery after lung resection and presented 15 cases of their own showing that women who have had surgery of the lung do well obstetrically. In six of their patients who were operated upon during gestation there was one abortion, one death due to empyema and four normal deliveries. Schaefer and Epstein[19] also reported two cases who did well, in whom surgery was done during pregnancy. Similarly Schaefer *et al.*[20] reported 298 deliveries in 257 patients; 29 of whom had major thoracic surgery for tuberculosis. In the present series all of the patients who received surgical treatment were operated upon after delivery. There was one who had pneumonectomy for tuberculosis and she became pregnant subsequently and delivered normally.

SUMMARY

This report deals with 53 patients in whom pregnancy and active tuberculosis coexisted compared with 53 non-pregnant patients with active tuberculosis who were of the same age group and disease status.

There was no significant difference in the groups in sputum conversion, roentgenographic improvement and stabilization, cavity closure, or rate of relapse, either early or late. This is in accordance with other recent studies which show that pregnancy has no deleterious effect on tuberculosis when the infection is treated with adequate and prolonged chemotherapy and surgical procedures when indicated. It also stresses the importance of ante-natal radiographs of the chest.

RESUMEN

Esta comunicación trata de 53 enfermas en quienes coexistía embarazo y tuberculosis activa comparándolas con 53 enfermas no embarazadas con tuberculosis activa del mismo grupo de edad y estado de su enfermedad pulmonar.

No hubo diferencia significativa en cuanto a conversión de esputos, mejoría radiográfica y estabilización, cierre de cavernas o proporción de recaídas ya fuesen tempranas o tardías. Esto está de acuerdo con otros estudios recientes que muestran que el embarazo no tiene efecto perjudicial sobre la evolución de la tuberculosis cuando la infección es tratada de manera adecuada y con la quimioterapia prolongada y la cirugía cuando está indicada. Esto también destaca la importancia de las radiografías prenatales del tórax.

RESUMÉ

Cette comunication concerne 53 malades chez lesquelles coexistaient une grossesse et une tuberculose active, comparées à 53 malades non enceintes, atteintes de tuberculose évolutive, qui appartenaient au même groupe d'âge et de condition pathologique.

Il n'y eut aucune différence marquée dans les groupes en ce qui concerne la négativité de l'expectoration, l'amélioration radiologique et la stabilisation, la fermeture des cavités, ou le taux de rechute, soit précoce, soit tardif. Ceci s'accorde avec d'autres études récentes, qui montrent que la grossesse n'a pas d'effet fâcheux sur la tuberculose, quand l'infection est traitée par une chimiothérapie appropriée et prolongée, ainsi que par les moyens chirurgicaux s'ils sont indiqués. Ceci met en lumière l'importance des radiographies thoraciques avant l'accouchement.

ZUSAMMENFASSUNG

Dieser Bericht betrifft 53 Kranke, bei denen gleichzeitig eine Schwangerschaft und eine aktive Tuberkulose bestand, im Vergleich mit 53 nicht schwangeren Patienten, mit aktiver Tuberkulose, die der gleichen Altersgruppe und demselben Krankheitszustand bugehörten.

Es ergab sich kein entscheidender Unterschied zwischen beiden Gruppen hinsichtlich der Bazillenfreiheit, röntgenologischen Besserung und Stabilisierung, Cavernenverschluß sowie Häufigkeit von Früh- oder Spät- Recidiven. Diese Beobachtung stimmt mit anderen jüngeren Untersuchungen überein; sie zeigen, daß die Schwangerschaft keinen nachteiligen Einfluß auf die Tuberkulose ausübt, sofern diese mit entsprechender und genügend lange durchgeführter Chemotherapie und chirurgischen Maßnahmen, falls diese indiziert sind, behandelt wird. Ferner wird die Wichtigkeit von Thoraxröntgenaufnahmen vor der Entbindung hervorgehoben.

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A New Vista in Pulmonary Cytology; Aerosol Induction of Sputum

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Artificial induction of sputum has not only increased the accuracy of pulmonary cytology in the diagnosis of bronchial carcinoma, but has broadened the scope of its applicability. Now, for the first time, the potentiality of sputum examination in detecting early carcinoma or premalignant bronchial changes in asymptomatic persons is ready for evaluation.

There are four principal methods for obtaining bronchial secretions: (1) spontaneous or "natural" cough; (2) bronchial aspiration via the bronchoscope; (3) stimulation of the cough reflex by irritative inhalants; and (4) instrument-less flushing of the lower respiratory tract by aerosolized solutions. The last method has been devised and perfected by Bickerman and associates[1] who found that the inhalation of hygroscopic saline-aerosol, heated above body temperature, and delivered in small droplets, provided maximum intra-bronchial "rain-out." Using this technic, they were able to produce sputum in 86 per cent of patients who had no cough or who could not raise sputum. Other investigators using this method reported an increase in the sensitivity of the cytologic diagnosis from less than 70 per cent to over 85 per cent in a small series of bronchial carcinomas.[2]

This report concerns the application of the method of Bickerman *et al.* to the routine hospital practice of exfoliative cytology. The potentialities of this procedure in the detection of early carcinoma or premalignant lesions will be discussed.

Material and Method

Artificial induction of sputum (AIS) was not used for those patients whose spontaneous sputum contained malignant cells. The patients whose sputum was induced were divided into three groups according to the nature of their spontaneous sputum:

1. Unsatisfactory	(31 patients)
2. Negative	(57 patients)
3. Equivocal	(17 patients)
TOTAL	105 patients

The criterion for a satisfactory specimen was the presence of alveolar macrophages ("dust-cells"). Equivocal specimens were those containing cells which were reported as suspicious or atypical.

There were 273 AIS examinations in the 105 patients, the number per patient varying from one to eight. During this same period, 820 spontaneous sputa were submitted for cytologic examination, and 84 bronchial aspirates were examined.

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The hygroscopic saline-aerosol technic of Bickerman *et al.*[1] was used. The inhalation was maintained for 10 to 20 minutes and the average amount of nebulized fluid used was 10 to 15 ml. The sputum was expectorated directly into an ether-alcohol mixture. A mean quantity of 10 ml. of sputum was obtained, and in no instance was less than 5 ml. collected. The smears were stained according to the standard Papanicolaou procedure.

Results

Adequacy of Specimens:

Among the 820 spontaneous sputa, 336 (41 per cent) were regarded as inadequate because of complete lack or insufficient numbers of "dust-cells" indicating insufficient bronchial secretions. Suitable specimens were obtained by AIS from 29 of the 31 patients who had been unable to raise sputum containing bronchial secretions. The AIS specimens compared favorably with *satisfactory* spontaneous sputa. The former contained more bronchial columnar cells, more pulmonary histiocytes, and fewer cells or debris from the oral cavity and upper respiratory tract.

Fifty-seven (68 per cent) of the 84 bronchial aspirates or washings were satisfactory for cytologic examination, but smears from AIS specimens almost invariably contained more "dust-cells" than did bronchial aspirates, and fewer columnar cells.

Diagnostic Sensitivity:

Among the 57 patients who had AIS because of negative smears, and the 31 who had unsatisfactory spontaneous cough specimens, were 29 who eventually proved to have bronchial carcinoma. Malignant cells were recovered from 20 (69 per cent) of these 29 patients by AIS, despite repeated failures with the "natural cough" specimens. In several instances, the spontaneous sputum specimens which had been negative prior to AIS became positive following this procedure. This suggested that the inhalation of the mucolytic propylene glycol released impacted mucous plugs which had prevented the egress of the carcinoma cells.

Bronchial aspirates had been examined from 12 of the same 29 patients, and only four contained carcinoma cells.

Among the 17 patients who had *equivocal* cytologic reports on the basis of examination of sputum collected by the conventional method, AIS provided sufficient supplemental information in seven instances to permit a more definite categorization, either positive or negative.

Discussion

Cytologic examination of bronchial aspirates greatly increases the diagnostic value of bronchoscopy, and specimen for specimen, bronchial aspirates are superior to spontaneous sputum in the diagnosis of bronchogenic carcinoma. Smears from these aspirates may be screened more rapidly because there is less contamination by cells and debris from the oral cavity and the upper respiratory passages. There are, however, two disadvantages of bronchial washings: one is that it is seldom convenient to obtain a repeat specimen, as it is with sputum samples; the other is the frequent failure to obtain malignant cells from lesions which are located in the smaller rami of the respiratory tree. This may be due to bronchospasm incident to the trauma of bronchoscopy, which may also explain the relatively small number of "dust-cells" present in smears from this material.

The results reported here indicate that the secretions obtained in aerosol-induced sputum are superior not only to spontaneously raised sputum, but also to bronchial

aspirates. To date, we have used this new procedure only to complete the cytologic profile of patients under study because of strong clinical or roentgenographic evidence of bronchial carcinoma. However, it is apparent that much time could be saved by applying this procedure immediately, without attempting to collect sputum by the conventional technic. This would shorten expensive diagnostic hospitalization and decrease the workload of the cytologic laboratory, since the number of specimens examined can be reduced. Recently, we recommended the use of AIS as an office or out-patient department procedure for the rapid diagnosis of bronchial carcinoma.[3] The apparatus is inexpensive and is simple to operate. It may be repeated as often as desired since it does not produce discomfort. In fact, many patients obtain relief of their respiratory symptoms due to the mucolytic activity of the inhalant.

There is at present an urgent need for applying this diagnostic modality to the early detection of bronchial carcinoma, to the screening of asymptomatic populations, and to the study of premalignant alterations of the bronchial mucosa. There is considerable pessimism regarding the ability of current diagnostic modalities for the detection of *curable* bronchial carcinoma. This pessimism has been based largely upon the inability of annual or semi-annual x-ray film examination of the chest to detect most early bronchial carcinomas. The development of metastases from small primary neoplasms has also been cited as additional justification for this lack of enthusiasm. Nevertheless, we have little knowledge concerning the incidence or duration of premalignant bronchial changes or intraepithelial carcinoma of the bronchus. The significant work of Auerbach and associates[4] and the observations of Knudtson[5] suggest that premalignant alterations and carcinoma-*in-situ* are common, especially in heavy smokers, and may be present for some time before developing into invasive carcinomas. The exhaustive studies on carcinoma-*in-situ* of the cervix uteri have highlighted the long period between latent and invasive carcinoma.

AIS provides the means to explore the cytologic manifestation of bronchial dysplasia and early neoplasia, just as cervical smears have elucidated the comparable alterations in the cervix uteri. We have encountered atypical squamous cells and bizarre hyperplastic columnar cells in the sputum of heavy smokers who have no roentgenographic evidence of lung disease. These cells probably represent the cytologic equivalent of the mucosal atypia reported in histologic studies.[4,5] The potential value of the AIS in the detection of early bronchogenic carcinoma or in premalignant lesions of the bronchial mucosa has been recognized. Its use in the early detection of bronchial carcinoma is currently being evaluated.[6]

SUMMARY AND CONCLUSIONS

Hygroscopic, heated, saline-aerosol induction of sputum provides specimens which are superior to spontaneously raised sputum or bronchial aspirates for the cytologic diagnosis of bronchial carcinoma.

This new technic not only increases the sensitivity of the cytologic diagnosis of bronchogenic carcinoma, but provides the means for studying cells from bronchial dysplasia and early neoplasia. Studies are needed to determine the feasibility of using this procedure for detecting premalignant or early malignant changes in the bronchial mucosa.

The method is recommended for routine hospital, out-patient, and office practice. It may very well become a part of routine periodic examination as are roentgenograms of the chest and electrocardiographic examination of the heart.

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RESUMEN Y CONCLUSIONES

La aplicación de aerosol salino, higroscópico y caliente, permite la provocación de esputos que son superiores a los emitidos espontaneamente o a las aspiraciones bronquiales para el estudio citológico y diagnóstico del carcinoma bronquial.

Esta técnica nueva no solo aumenta la exactitud del diagnóstico citológico del carcinoma bronquiogénico sino que proporciona medios para estudiar celdillas distinguiéndo la displasia bronquial y la neoplasia temprana.

Se necesitan estudios para determinar la practicabilidad de este proceder y para descubrir cambios premalignos o malignos tempranos en la mucosa bronquial.

El metodo se recomienda para la rutina de hospital, servicio externo y para el consultorio. Bien puede venir a ser una parte del exámen de rutina periódico como la roentgenografía del torax y el exámen electrocardiográfico para las enfermedades del corazón.

RESUMÉ

La provocation de l'expectoration par un aérosol salin, hygroscopique, chauffé, permet d'obtenir des échantillons qui sont supérieurs à l'expectoration éliminée spontanément, ou aux aspirations bronchiques, pour le diagnostic cytologique du cancer bronchique.

Cette nouvelle technique n'augmente pas seulement la sensibilité du diagnostic cytologique de cancer bronchique, mais donne les moyens d'étudier les cellules provenant de dysplasie bronchique et de néoplasie à leur extrême début. Des études sont nécessaires pour déterminer la facilité de l'utilisation de cette technique pour détecter les modifications pré-malignes ou précocement malignes de la muqueuse bronchique.

La méthode est recommandée pour la pratique hospitalière, le malade soigné en ville, et le cabinet du médecin. Il peut très bien devenir une partie de l'examen systématique périodique comme le sont les radiographies du thorax et l'examen électrocardiographique du coeur.

ZUSAMMENFASSUNG UND SCHLUSSFOLGERUNGEN

Gewinnung von Sputum durch hygroskopische erhitzte Salzlösung im Aerosolverfahren führt zu Präparaten, die einem spontan entleerten Sputum oder Bronchialsekret für die cytologische Diagnose des Bronchialkrebses überlegen sind.

Diese neue Technik verbessert nicht nur die Empfindlichkeit der cytologischen Diagnose beim bronchogenen Karzinom, sondern liefert auch das Material zum Studium von Zellen bei einer Dysplasie und frühen Neoplasie der Bronchialschleimhaut. Weitere Untersuchungen sind erforderlich zur Bestimmung, ob es möglich ist, diese Methode dazu zu benutzen, noch nicht bösartige oder gerade eben frühzeitig bösartig gewordene Veränderungen in der Bronchialschleimhaut aufzufinden.

Das Verfahren wird empfohlen zur routinemässigen Anwendung in Krankenhäusern, bei ambulanten Patienten und in der Sprechstunde. Es kann sehr wohl zum Teil einer routinemässigen periodischen Untersuchung werden, wie es die Thoraxröntgenaufnahmen und die elektrocardiografischen Herzuntersuchungen bereits sind.

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SURGERY FOR HIATUS HERNIA AND ESOPHAGITIS

This report is based on studies (135) consisting of simultaneous measurement of pH and pressure in the area of the esophagogastric junction performed on 104 subjects. A measurement of the pH in the terminal esophagus gives the surgeon an accurate estimate of the presence and severity of peptic activity in this area. These studies have been of value as a diagnostic tool in those patients in whom x-ray has failed to demonstrate either a hiatus hernia or regurgitation, but who are suffering with severe symptoms. We feel that this is particularly important because it is in this group of patients with no demonstrable hernia or with a small hernia in whom many diagnostic errors are made. It is in this group that many of the poor surgical results obtained in the past have occurred, since the symptoms in these patients may be confused with a number of other disorders. These studies have also been of value in assessing the effect of surgical treatment upon the underlying pathophysiology. In those patients who had an adequate operation and who were studied postoperatively, complete correction of the tendency to reflux could be demonstrated. In those patients with only simple closure of the hiatus and no additional sutures to re-construct the gastroesophageal angle, or to hold the stomach in its position below the diaphragm, continued regurgitation was demonstrated, either clinically or experimentally, in seven patients, indicating that simple closure of the hiatus is an inadequate procedure for hiatus hernia and esophagitis.

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Effect of Changes in Arterial pH on the Action of Adrenalin in Acute Adrenalin-Fast Asthmatics*

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There is probably no field of medicine in which drugs can do more to comfort, though not cure, the patient than in asthma. There is nothing more disturbing than to find that adrenalin, the drug which is still by far the best in the treatment of acute allergic states, is losing its effectiveness. It is so easy to understand the apprehension, even the panic which so often communicates itself to those about him, which the patient feels when he realizes what is happening. He then tries to hyperventilate, but only succeeds in getting more air into an already overdistended lung, air which is trying to get out through narrowed openings and aggravating by increased pressure, particularly on the small bronchioles that have lost their cartilagenous support, the other findings in acute allergic asthma—the edema, and the extremely important and probably the fundamental problem in treatment, the thick tenaceous secretion. This is the more important in that adrenalin fastness occurs more readily, certainly more frequently, in so-called intrinsic asthma, where the emotional element and probably, therefore, the spastic element, is so often of great importance. There have been a great many explanations for this. The most acceptable are, first, that in these people adrenalin continues to have the effect of increasing pulmonary pressure, but has lost the ability to dilate the bronchioles. Second, their cells do not or do not readily oxidise adrenalin. Both explanations obviously beg the question. A few years ago Dr. G. S. Campbell, in a thesis on cardiac arrest in surgery, called attention to the fact that in the acute respiratory acidosis induced by general anasthesia, adrenalin has little effect. It then occurred to one of us (J.S.B.) that here must be at least in part, an answer to adrenalin fastness. A review of the literature by the authors failed, however, to reveal anything in clinical literature correlating the arterial pH with the action of adrenalin in acute respiratory acidosis certainly in asthmatics. There are probably some good reasons for this. First, the patient is so acutely ill that the clinician is naturally loathe to procrastinate, to order what he deems to be unnecessary laboratory procedures, and to delay therapy which, in the past, and probably by means other than purely relief of smooth muscle spasm, has restored these people to adrenalin sensitivity. Secondly, and probably much more important, until recently arterial pH was but infrequently done in private hospitals and almost as rarely in teaching institutions. The usually ordered CO_2 combining power all too often gives but little help as to the true status of arterial pH. Be that as it may, a review of the literature in physiology reveals that a vast amount of work has been done in this field. This points up the fact that all too

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often work done in one discipline of medicine is disregarded, certainly not emphasized, in others.

Mathews,[1] in 1916, noted that oxidation of epinephrine was "hastened by alkalies." Snyder and Andrus[2] concluded that "the effect of ephinephrine upon the terrapin heart is in part a function of the H ion concentration of the perfusate." Snyder and Campbell[3] in 1920 stated that there was increased vasoconstriction as the pH of the perfusing fluid rose. McCarrison[4] noted the effects of asphyxia in the epinephrine-iris-light sensitivity reaction in the enucleated eye of the toad. The action was poor in the later stages of asphyxia and was said to be due to increased acidity of the blood. Alpern and Sorkin[5] in 1925 perfused the isolated rabbit's ear with epinephrine in Locke-Ringer's solution in different H ion concentrations and found increased effect with increased pH up to 8.1. Salent and Johnston[6] in 1924, working on the frog's heart, found decreasing effectiveness with decrease in pH until, in 6.5 to 6.7, stimulation was small and transitory. Burget and Visscher[7] in 1927, working with pithed cats and keeping artificial respiration constant, found that small intravenous injections of epinephrine act with progressively increasing effectiveness, provided the pH of the blood is rising. They concluded that this was not due to the drug's sensitizing the sympathetic nervous system. It seemed to be due either to an increased irritability of the sympathetic nervous system as a result of the increased pH, or rise in pH causing epinephrine to be oxidized more completely and rapidly. Beznak[8] in 1934 found, on the other, hand, that frogs' hearts at pH 7.8 were resistant to repeated application of acetylcholine, but as the pH was shifted toward the acid state, the effects were increased. Campbell[9] in 1950 states that cardioinhibitory effects resulting from faradic vagal stimulation and intravenous acetylcholine were increased in dogs with a lowered pH. That the effects may not be due entirely to the systemic pH is suggested by the work of Clark.[10] He notes that digestion in cells results in acid products which attract fluid, leading to edema, anoxia, and further acidity. The pituitary-adrenal-thyroid glands stimulate alkalinization, but this is limited due to their own share in general anoxia acidosis. Repeated exposure to allergens, as in asthma, may diminish response in part because of reduction in available alkaline reserve. Barcroft[11] in 1955, working on voluntary human sub-

TABLE 1—PRESSOR RESPONSES BEFORE, DURING AND AFTER RESPIRATORY ACIDOSIS IN INTACT DOGS

	Pre-Acidosis		Respiratory Acidosis		Post-Acidosis	
	Pre-injection B. P. (mm.Hg.)	Post-injection B.P. increased (per cent)	Pre-injection B. P. (mm.Hg.)	Post-injection B.P. increased (per cent)	Pre-injection B. P. (mm.Hg.)	Post-injection B.P. increased (per cent)
Epinephrine	139	36	133	18	117	38
Norepinephrine	131	57	133	29	122	34
Neosynephrine	131	52	146	16	142	14
Cobefrin	124	61	116	65	122	64
Aramine	122	59	142	21	128	28
	pH=7.34*		pH=6.76*		pH=7.27*	

*Average values for 5 dogs.

jects, noted that epinephrine in man stimulated respiration and the pH instead of becoming more acid actually became more alkaline during stimulation. This, it seems to us, points up the importance in nature of an alkaline media for the best action of epinephrine. In 1954, Campbell *et al.*[13] found that the alteration in the cardio-inhibitory effects of either faradic vagal stimulation or acetylcholine in dogs can be correlated with changes in blood pH.

While observing the action of vasopressor agents in our own physiology laboratories, Houle[12] *et al.* subjected five intact dogs to respiratory acidosis by inhalation of 30 per cent CO_2 and 70 per cent O_2. Blood pressure, ECG, arterial blood for pH were recorded. Epinephrine and other sympathomimetic agents were given intravenously through a femoral vein catheter. Adrenalin in doses of 2.7 per kg. was used. Ventricular extrasystoles, ECG changes and tachycardia were noted in control pH more marked than in acidotic dogs. The pressor response to adrenalin was also reduced from an average of 36 per cent pre-acidosis at pH 7.34 to 18 per cent in acidosis at pH 6.76 and again to 38 per cent post acidosis at pH 7.27.

To get away from the ventricular extrasystoles, cardiac by-pass was done in 10 dogs.

TABLE 2—PRESSOR RESPONSES BEFORE, DURING AND AFTER RESPIRATORY ACIDOSIS IN CARDIAC BY-PASS DOGS

	Pre-Acidosis		Respiratory Acidosis		Post-Acidosis	
	Pre-injection B. P. (mm.Hg.)	Post-injection B. P. Increased (per cent)	Pre-injection B. P. (mm.Hg.)	Post-injection B. P. Increased (per cent)	Pre-injection B. P. (mm.Hg.)	Post-injection B. P. Increased (per cent)
Epinephrine	89	63	104	19	80	32
Norepinephrine	113	57	119	26	116	21
Neosynephrine	102	83	91	33	79	50
Cobefrin	98	80	86	37	53	52
Aramine	119	65	125	12	126	26
	pH=7.37*		pH=6.68*		pH=7.13*	

*Average values for 5 dogs.

The root of the aorta and pulmonary artery were clamped. In these dogs the pre-acidosis increase in blood pressure to adrenalin was 63 per cent at pH of 7.37, 19 per cent in acidosis at pH of 6.68 and 32 per cent in post-acidosis at pH of 7.13.

As we were primarily interested in the response of respiratory smooth muscle to adrenalin, the guinea pig, an animal that responds most like the human to anaphylaxis, was used to note this effect. Unfortunately, it is difficult to work with this small and fragile animal. Adopting the technique of Castelle and deBeer,[14] Dr. Aryabala Prasad in our physiology department used the trachea of that animal. The trachea was divided into circular rings of equal size and a chain was made using 10 rings tied in a chain with 5-0 silk suture—like a child's ribbon. The chain was immersed in a glass container with 65 cc. of Chenoweth solution kept at a constant 38°C temperature. The rings of trachea were connected to a strain gauge for recording tension. The pH was lowered to 6.71 to 7.0 by

(a) running 30 per cent CO_2 and 70 per cent O_2 into a solution containing 25 mM./L. of $NaHCO_3$; (b) lowering the $NaHCO_3$ concentration of the solution to 3.43 mM./L. equilibrated with 5 per cent CO_2 and 95 per cent O_2; (c) addition of 1.2 NHCl to the solution containing 25 mM./L. of $NaHCO_3$ equilibrated with 5 per cent CO_2 and 95 per cent O_2. The pH was increased to 7.6—8.1 by (a) adding 50 mM./L. $NaHCO_3$ to the solution equilibrated with 5 per cent CO_2 and 95 per cent O_2; (b) running 100 per cent O_2 into the solution containing 25 mM./L. of $NaHCO_3$. These experiments showed that the effect of adrenalin was much less marked in causing relaxation of tracheal guinea pig muscle in respiratory acidosis and more marked in alkalosis.

With these factors as a background, we decided to give adrenalin intravenously to human volunteers and vary the arterial pH. We were, of course, fully cognizant of the extreme danger of I.V. adrenalin in humans—ventricular fibrillations, C.V.A., and damage to the heart, the liver and the kidneys by vasopressor agents. Two healthy non-anesthetized subjects were so studied. They were laid on a table in the physiology laboratory. The arterial blood pressure was taken with a pressure transducer connected to a needle in the brachial artery and recorded on one channel of a direct-writing Sanborn. Another channel was used to record the second lead of the electrocardiograph. Minute respiratory volumes were measured by the open circuit method using a modified A-15 Army aviation mask. The exhaled air was collected in a 100 liter balanced spirometer. Ten per cent CO_2—90 per cent O_2 was used to produce acidosis and voluntary hyperventilation akalosis. They were watched as to clinical effects, blood pressure, rate, ECG. Arterial blood was obtained from the brachial artery for pH and total carbon dioxide content determinations. Carbon dioxide tension, carbonic acid concentration, and bicarbonate concentration were obtained by using the Henderson-Hasselbolch equation. The subjects were connected to an intravenous drip which was also used to give intravenous adrenalin during the experimental periods.

TABLE 3—CASE 1

	CO_2	pH	p CO_2	Rate Before Epinephrine	Rate After Epinephrine
Control room air	26.8 mm.	7.36	47.5	60	114 (¼ cc. 1/10,000)
10 per cent CO_2	29.4 mm.	7.25	66.0	114	128 (¼ cc. 1/10,000)
Hyperventilation	20.6 mm.	7.61	20.9	114	156 (⅛ cc. 1/10,000)
			CASE 2		
Control room air	26.4 mm.	7.38	45.0	60	96 (0.3cc. 1/20,000)
10 per cent CO_2	31.3 mm.	7.22	75.0	90	96 (0.3cc. 1/20,000)
Hyperventilation	21.3 mm.	7.60	22.0	55	114 (0.3cc. 1/20,000)

The results are noted in Table 3. In case 1, ¼ cc. of 1/10,000 adrenalin changed the heart rate from 60/114 per minute. In respiratory acidosis (pH 7.25), the same dose, the rate changed from 114 to 128 per minute only. In respiratory alkalosis (pH 7.61) the dose of adrenalin, because of our own apprehension, was halved to ⅛ cc. of 1/10,000, but the rate increased from 114 to 156 per minute. In case 2, 0.3 cc. of 1/20,000 adrenalin showed a rate change in eupnea at pH of 7.38 from 60 to 96;

in respiratory acidosis at pH of 7.22 from 90 to 96 only; and in alkalosis at pH 7.60 from 55 to 114. Of great significance was the more marked changes in the ECG, ventricular extrasystoles and marked T wave changes noted, during alkalosis. The greater effectiveness of adrenalin in a higher pH was evident.

With these findings as a background, we decided to give intravenously one molar sodium lactate to adrenalin-fast or adrenalin-resistant patients in asthmatic states. Forty-five patients have been so treated with dosage from 120 to 300 cc. given in a period of about 30 minutese. We had learned, in previous clinical and laboratory studies, that to be effective the solution must be given fairly rapidly in concentrated solution and early, before the thick tenanous secretions become increasingly more important than muscle spasm. No other medication to start was given. The results were apparently due to the increased effectiveness of the patients' endogenous adrenalin. We had arterial pH in 10 cases—ranging from 7.26 to 7.32 before therapy and 7.39 to 7.45 after molar sodium lactate. The results were good within a period of time, ranging from 10 minutes to several hours. The response was at times rapid and dramatic so that we believed that something other than systemic pH might be involved —possibly local tissue acidosis as suggested by Clark. Be that as it may, the relief of symptoms was gratifying in cases where it was desperately needed. While it is true that allergic asthmatics will frequently respond to simple measures like mere change of environment to avoid allergens, reassurance, sedation, and fluids, it is equally clear that the type of patients referred to here do not respond so readily or so easily.

Case Reports

Case 1: J.G., a 45-year-old man, gave a history of perennial asthma of 20 years aggravated by exertion, change of temperature, and upper respiratory tract infections. Epinephrine nebulization gave relief unless attacks were prolonged, then no effect was obtained. Many allergic regimes including change of climate, diets, and desensitization, were tried with no permanent relief. He was fairly comfortable between acute episodes. He had been hospitalized many times in asthmatic states during which the usual therapy with aminophyllin, oxygen, intravenous fluids, etc., gave relief after a few days. He would then become again epinephrine-sensitive. During admission described, his pH was 7.30 and his CO_2 32. He was in status asthmaticus and epinephrine resistant. Intravenous molar sodium lactate, 120 cc. gave marked relief in one hour. No other medication was given. His pH rose to 7.39 and he was asymptomatic the next day. The results were much more complete and faster than in other past episodes with other routines.

Case 2: A.K., a 49-year-old married woman, gave a history of asthma since age 19. She had perennial symptoms aggravated by colds, emotional episodes, dust, and penicillin. Many usual therapeutic regimes gave temporary relief, including epinephrine by spray and parenterally for her attacks. This gave marked relief except during severe episodes when it had no effect, either parenterally or by inhalation. Numerous hospitalizations lasting up to two weeks gave her remission with the use of rest, aminophyllin, sedative, intravenous glucose, and oxygen. ACTH and cortisone had been given in the last few years with good results but marked emotional disturbances. During her last hospital admission she was in status asthmaticus and was epinephrine-fast. The blood pH was 7.27 and CO_2 26. Intravenous sodium lactate was given. In about 20 minutes, before a total of 120 cc. had been given, the patient noted marked relief, much more than with any other of the many procedures previously used in her long history. She had a little wheezing the next few days, which responded promptly to epinephrine by inhalation.

SUMMARY

1. The physiology literature since 1916 has pointed out the increased effect in animals of adrenalin in an alkaline medium and the decreased effect in acidosis particularly on blood pressure, rate and electrocardiogram.

2. Changing the pH to the acid side by CO_2 inhalation resulted in a markedly decreased effect of adrenalin both in the intact and cardiac by-passed dogs.

3. Circular rings of guinea pig trachea, tied together and immersed in solution, responded to adrenalin with increased dilation when the solution was made more alkaline and less so when the pH was lowered.

4. Intravenous adrenalin was given to human volunteers. Arterial pH was changed to the alkaline side by voluntary hyperventilation and to the acid side by CO_2 inhalation. The response to adrenalin on blood pressure, rate, ECG was markedly increased as the pH was elevated.

5. It would seem that asthmatics may at least, in part, become "adrenalin fast" because of respiratory acidosis. Forty-five "adrenalin-fast" asthmatics were, therefore, given one molar sodium lactate in dosage of 120 to 300 cc. intravenously. Arterial pH was obtained in 10 cases and ranged from 7.26 to 7.32 before therapy and 7.39 to 7.45 after. The results were good when the molar lactate was given early, rapidly and before the thick, tenaceous sputum became more important than the smooth muscle spasm.

6. Molar sodium lactate seems to be the drug of choice in adrenalin fast asthmatics except where contraindicated because of the danger of sodium retention as in nephritis, cardiac decompensation, tetany and possibly the previous use of large doses of steroids. The results seem to be due to the increased effect of adrenalin in more alkaline media, increased sensitivity of the sympathetic to adrenalin in a more alkaline medium or decreased effect of acetylcholine.

RESUMEN

1. La literatura de fisiología desde 1916 ha señalado el aumento del efecto de la adrenalina en los animales en medio alcalino y el decrecimiento en la acidosis, especialmente en la presión arterial, frecuencia y en el electrocardiograma.

2. Cambiando el pH a la acidez por la inhalación de CO_2 se obtuvo un decrecimiento del efecto de la adrenalina tanto en los perros no modificados como en los que tienen una desviación cardiaca.

3. Los anillos circulares de la tráquea de cuyes, atados y sumergidos en solución respondieron a la adrenalina con una dilatación mayor cuando la solución era alcalina y menos cuando el pH se hizo descender.

4. Se inyectó adrenalina intravenosa a voluntarios. El pH arterial se cambió a alcalino por la hiperventilación voluntaria y hacia la acidez por la inhalación de CO_2. La respuesta de la adrenalina sobre la presión arterial, frecuencia y ECG fué marcadamente mayor a medida que el pH se elevaba.

5. Parece que los asmáticos pueden cuando menos en parte, hacerse "adrenalino-resistentes" por la acidosis respiratoria.

Por tanto, se proporcionó a cuarenta y cinco asmáticos "adrenalino-resistentes" lactato de sodio molar a la dosis de 120 a 300 c.c. intravenosamente. El pH arterial se obtuvo en 10 casos y fué de 7.26 a 7.32 antes del tratamiento y de 7.39 a 7.45 después. Los resultados fueron buenos cuando el lactato molar se dió tempranamente rápidamente y antes de que el esputo espeso y adherente fuese mas importante que el spasmo del músculo liso.

6. El lactato de sodio molar parece ser la droga de elección en los asmáticos resistentes a la adrenalina excepto cuando hay contraindicación por el peligro de retención de sodio como en las nefritis, descompensación cardiaca, tetania y probablemente cuando antes se han usado grandes dosis de esteroides. El resultado parece deberse al aumento de la acción de la adrenalina en los medios mas alcalinos, el aumento de la sensibilidad simpática de la adrenalina en un medio mas alcalino o el efecto disminuido de la acetilcolina.

RESUMÉ

1. La littérature sur la physiologie a mis l'accent depuis 1916 sur l'augmentation de l'effet de l'adrénaline en milieu alcalin chez les animaux, et la diminution de l'effet dans l'acidose, particulièrement sur la pression sanguine et l'électrocardiogramme.

2. Le virage du pH dans le sens acide par inhalation de gaz carbonique provoque une diminution nette de l'activité de l'adrénaline aussi bien chez les chiens normaux que chez ceux qui ont une circulation extra-cardiaque.

3. Des anneaux circulaires de la trachéa de cobayes, liés ensemble et immerfiés dans une solution, répondirent à l'adrénaline, avec augmentation de la dilatation quand la solution était plus alcaline et moindre quand le taux du pH était abaissé.

4. De l'adrénaline intra-veineuse a été administrée chez des témoins volontaires. Le taux du pH artériel fut modifié dans le sens de l'alcalinité par hyperventilation volontaire et dans le sens de l'acidité par inhalation de gaz carbonique. La réponse à l'adrénaline sur la pression sanguine et l'électrocardiogramme fut nettement augmentée lorsque le taux du pH était élevé.

5. Il semblerait que les asthmatiques pourraient au moins en partie, devenir "résistants à l'adrénaline" par acidose respiratoire. 45 asthmatiques, "résistants à l'adrénaline," reçurent une solution molaire de lactate de sodium à la dose de 120 à 300 cc. par voie intra-veineuse. Le pH artériel fut calculé dans 10 cas et atteignait 7,26 à 7,32 avant traitement et 7,39 à 7,45 après. Les résultats furent bons lorsque le lactate molaire fut donné précocément, rapidement, et avant que l'expectoration épaisse ne devint plus importante que le spasme des muscles lisses.

6. Le lactate de sodium en solution molaire semble être le produit de choix chez les asthmatiques résistants à l'adrénaline, sauf lorsqu'il y a une contre-indication due à la rétention de sodium comme dans la néphrite, la décompensation cardiaque, la tétanie et également l'utilisation antérieure de doses massives de stéroïdes. Les résultats semblent être dus à l'augmentation de l'effet de l'adrénaline dans un milieu plus alcalin, à l'augmentation de la sensibilité du sympathique à l'adrénaline dans un milieu plus alcalin ou un effet dépresseur de l'acétylcholine.

ZUSAMMENFASSUNG

1. Die physiologische Literatur hat seit dem Jahre 1916 den verstärkten Einfluß von Adrenalin auf Tiere in einem alkalischen Medium hervorgehoben und den verringerten Effekt bei Acidose, besonders was Blutdruck, Pulsgeschwindigkeit und Elektrocardiogramm angeht.

2. Eine Veränderung des pH nach der saueren Seite durch CO_2-Inhalation hatte eine ausgesprochene verringerte Wirkung des Adrenalin zur Folge, sowohl bei intaken wie auch bei cardial kurz geschlossenen Hunden.

3. Zirkuläre Ringe der Meerschweinchen-Trachea zogen sich zusammen und gingen in Lösung, reagierten auf Adrenalin mit zunehmender Dilatation, wenn die Lösung alkalischer wurde, und mit herabgesetzter Dilatation, wenn der pH-Wert erniedrigt wurde.

4. An Freiwillige wurde intravenös Adrenalin verabfolgt. Der arterielle pH-Wert wurde mehr alkalisch gemacht durch absichtliche Hyperventilation und mehr sauer durch CO_2-Inhalation. Die Reaktion des Adrenalins auf Blutdruck, Puls und EKG wurde beträchtlich erhöht in dem Maße, wie der pH-Wert in die Höhe ging.

5. Es hat den Anschein, daß asthmatische Patienten, wenigstens teilsweise, "Adrenalin-fest" werden infolge einer respiratorischen Acidose. Es erhielten daher 45 "Adrenalin-feste" Asthmatiker molares Natriumlactat intravenös in einer Dosierung von 120 bis 300 ccm. Es wurden arterielle pH-Werte bestimmt in 10 Fällen, und sie lagen in der Höhe von 7,26 bis 7,32 vor der Therapie und schwankten zwischen 7,39 und 7,45 danach. Die Ergebnise waren gut, wenn das molare Lactat früh, schnell gegeben wurde, und ehe das dicke zähe Sputum mehr in den Vordergrund trat als der Spasmus der glatten Muskulatur.

6. Molares Natriumlactat scheint das Mittel der Wahl zu sein bei "Adrenalin-fasten" Asthmatikern, ausgenommen bei einer Kontraindikation wegen der Gefahr der Natriumretension wie bei Nephritis, cardialer Dekompensation, Tetanie und möglicherweise dem vorausgegangenen Gebrauch großer Dosen von Steroiden. Die Ergebnisse scheinen die Folge einer erhöhten Adrenalinwirkung in mehr als alkalischem Medium zu sein, einer verstärkten Sensibilität des Sympathicus auf Adrenalin in einem mehr alkalischen Medium oder dem verringerten Einfluß von Acetylcholin.

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A Long-Term Followup of 30 Neuropsychiatric-Tuberculosis Patients with the "Open-Negative" Syndrome of Indefinitely Prolonged Chemotherapy*

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Introduction

The phenomenon of the so-called "open negative" tuberculous cavity has become of increasing interest and concern in the past ten years and has been under investigation at many centers in regard to diagnosis, prognosis and treatment.[1] The present trend in the treatment of tuberculosis is a short term of hospitalization for the purpose of gaining control of the disease, education of the patient in the care of his disease, and such surgery as is indicated in individual cases. For this reason, the problem of management of patients with persistent tuberculous cavities, rendered not infectious by the use of anti-tuberculosis drugs, is of vital concern not only to physicians, but, from the standpoint of epidemiology, to public health authorities and, for socio-economic and psychological reasons, to patients and their families. We share the opinion of most students of tuberculosis that such cavities are potentially dangerous and have a great tendency to relapse and, therefore, should be resected whenever possible. However, there is no agreement in regard to the management of "open negative" tuberculous cavities in the not-inconsiderable number of patients whose cavities can not be resected, in poor surgical risk patients and in those who refuse surgery for any reason. In the meantime, physicians are faced with challenging questions and must treat these patients on the basis of the best information available.

The purpose of this presentation is to report the information and results of our study of 30 patients with "open negative" tuberculous cavities. These patients were observed while hospitalized under close medical supervision for periods ranging from two to over ten years as to the relationship between the duration of chemotherapy and the relapse rate and prognosis. The reported data form the basis for our present opinion that continuous tuberculostatic chemotherapy may prevent clinical relapses in the form of either positive bacteriology or further dissemination of the disease in the majority of patients who have become bacteriologically negative with apparent clinical healing.

Material, Criteria and Follow-up Methods

From 1947 through 1958, 450 patients have been treated by prolonged (over 18 months) chemotherapy in the neuropsychiatric-tuberculosis service of this hospital. The 30 reported on in this study represent those

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with the so-called "open negative" syndrome. All doubtful cases with roentgenographic evidence of air-containing defects without definite proof of tuberculous etiology were excluded in this series. They are all men, 26 white and four colored, ranging in age from 35 to 80 years (average age 60), eight with moderately, and 22 with far-advanced disease prior to chemotherapy. The criteria which we used for the selection and evaluation of patients is the same as that recently recommended by the Committee on Therapy of the American Trudeau Society:[8] (a) definite diagnosis of moderately or far-advanced tuberculosis, with radiographic evidence of cavitation confirmed by planigrams, and cultures positive for *Mycobacterium tuberculosis*; (b) persistence of cavitation and bacteriologic negativity, with serial x-ray film stability except for changes described in the paragraph on radiology, on prolonged use of anti-tuberculosis drugs; (c) arbitrarily chosen starting point of observation after 12 months of bacteriologic remission, during which time at least 24 gastric-contents cultures were done on each patient. Twenty-three were considered non-resectable and seven refused surgery. Four of the 23 cases improved sufficiently so that in two, unilateral resection, and in two others, extraperiosteal plombage was possible.

Treatment Methods

The majority of these patients were admitted to our service by transfer from other hospitals as (a) originally untreated; (b) re-treatment cases; or (c) therapeutic failures, the two latter groups having been previously treated with combined chemotherapy. Treatment regimens were selected or changed on an individual basis[3] taking into considera-

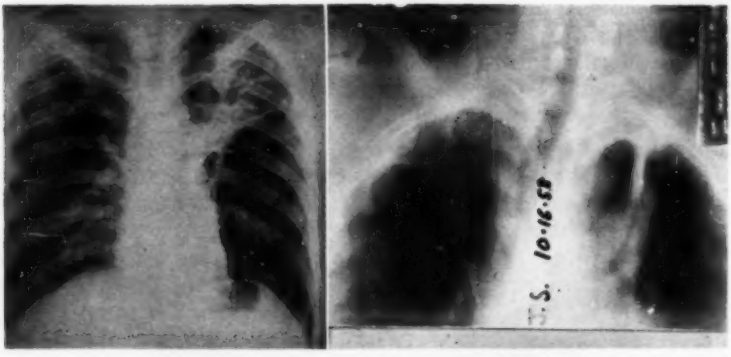

FIGURE 1A FIGURE 1B

FIGURE 1: R.J.S., white man born 1922; tuberculosis diagnosed in 1946; daily streptomycin given 5 weeks during 1948. Figure 1A. Chest x-ray film postero-anterior, April 8, 1952, showing widespread bilateral disease with a 6x7.5 cm. cavity, right upper lobe, and a 4x5 cm. cavity, left upper lobe, prior to combined chemotherapy. Bacteriology positive. Combined chemotherapy given from August, 1952 to August, 1954, re-started November, 1957, on admission to Downey. Last positive bacteriology November, 1955. Figure 1B. Tomogram, 9 cm. level, October, 1958, showing a bullous emphysema-like lesion, right upper lobe; shrinkage of left upper lobe lesion, with resultant cavity, 2 cm. in diameter, partially filled in. No further x-ray change. Combined chemotherapy given 36 months, INH alone 3 months. Expired September 20, 1959, of irreversible shock after abdominal surgery. Autopsy: Right upper lobe: healed cavity with clean fibrous wall. Left upper lobe: fibrocaseous tuberculosis, no macroscopic cavity. Bacteriology negative on tissue stain, cultures and guinea pig inoculation.

tion: (a) drug toxicity or intolerance; (b) resistance *"in vitro,"* apparent clinical resistance, or suspected biologic inactivation; (c) individual patients' lack of cooperation (drug refusal, etc.), and, (d) suspected or proved metabolic deficiencies. Two-drug antituberculosis regimens were given of the basic group: streptomycin, isoniazid, and para-amino salicylic acid. Three drug regimens were used for patients with toxic symptoms and progressive disease. In the event of bacteriologic resistance, toxic reaction, or intolerance to basic drugs, we used the supplementary drugs, pyrazinamide, viomycin, oxytetracycline, or cycloserine. (It is our experience that cycloserine, when judiciously used, is not contraindicated in neuropsychiatric-tuberculous patients. It was not given to patients who had history or clinical or encephalographic evidence of convulsive seizures). The drugs were used in recommended and usual in-practice dosage. Combined drugs were given from two to six years, depending upon the extent of disease and patients' response to treatment. After two to five years of negative bacteriology and radiographic stability, patients receive isoniazid alone, 300 mg. daily. At present, we have 17 patients on this regimen.

Laboratory and roentgenographic procedures consisted of those used by all study units in the Veterans Administration. Chest x-ray films are made at least at three-month intervals and planigraphic studies at least once a year. Two or three consecutive gastric-contents cultures monthly are taken for two to three years; after two years of bacteriologic negativity, two or three consecutive gastric-contents cultures are taken every four months. Susceptibility studies to drugs are done on streptomycin, isoniazid, para-amino salicylic acid, and cycloserine. Urinalysis, renal and liver function tests are done at least once monthly, as well as other tests, such as blood chemistry, audiometric studies, electroencephalograms and electrocardiograms as indicated.

Strict bed-rest, usually with bathroom privileges, was used in patients with toxic symptoms, then modified to partial bed-rest during their stay on the acute treatment service.

TABLE 1—BACTERIOLOGY (Closing Date October 30, 1959)

No. of Patients with Negative Cultures			Patients who had no record of Positive Bacteriology Prior to Treatment	Patients who had Single Positive Cultures Reported after Long Periods of Negativity
22 mos. to 3 yrs.	3 to 5 yrs.	5 to 8½ yrs.		
6	13	9	2	4
			H.W., tuberculosis confirmed on resected specimen.	F.G., single positive culture* after 39 months negativity.
			T.B., tuberculosis confirmed by a positive culture after 20 months chemotherapy.	J.K., single positive culture after 30 months negativity.
				S.D., single positive culture* after 36 months negativity and again 32 months later.
				T.B., never positive except for a single culture after 20 months combined chemotherapy.

*F.G. died nine months later and S.D. eight months later of cor pulmonale. At autopsy acid-fast organisms were found in tissue stains. Cultures and guinea pig inoculations were negative.

The majority of this group of patients has a history of chronic alcoholism, brain damage, and other co-existing organic diseases such as arteriosclerosis, cardiovascular and renal metabolic-endocrine dysfunction, and previous prolonged treatment with antituberculosis and tranquilizing drugs. Our experience shows that an increase in toxic reactions and hypersensitivity to drugs may be expected in this group.

Recent biochemical studies explain relationships between pharmacology, metabolism, and effectiveness and untoward reactions of antituberculosis drugs. Therefore, careful observation for symptoms and signs of clinical and subclinical deficiencies, toxic and allergic reactions[5] and drug intolerance is necessary and every effort is made to correct these states so as to influence favorably the individual patient's resistance factors, mental stresses included.[6]

Observations

Bacteriology: Fifteen patients obtained bacteriologic remission within the first year, 11 in from one to three years, and one after four and one-half years of individualized combined chemotherapy. Three turned negative prior to chemotherapy. Four had single positive cultures without x-ray shadow worsening (see Table).

Radiology: The observed patients have shown on serial roentgenograms: progressive resolution of the exudative component of infiltrations, regression of the pericavitary densities, shrinkage of the diseased areas, and diminution in size of cavities. The majority of patients have shown also secondary progressive compensatory sequelae of destruction

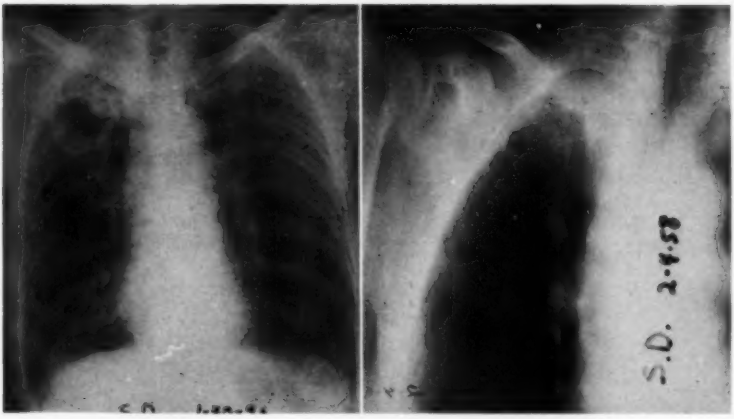

FIGURE 2A FIGURE 2B

FIGURE 2: S.D., white man born 1887; tuberculosis diagnosed in 1952; chemotherapy given June to October, 1952. Figure 2A. Chest x-ray film, January 30, 1953, showing bilateral disease with a cavity 6 cm. in diameter, right upper lobe, prior to re-treatment. Bacteriology positive. Combined chemotherapy re-started February, 1953. Considered a poor surgical risk. Figure 2B. Tomogram, 9 cm. level, February 4, 1958, showing resultant cystic-like open lesion 2 cm. in diameter, right upper lobe. Combined chemotherapy given 63 months, INH alone 13 months. Negative since February, 1953 except for single positive cultures in February, 1956 and October, 1958. Expired June 3, 1959, of cor pulmonale. Autopsy: Fibroid tuberculosis with minute caseous foci, right upper lobe; no macroscopic cavity. Pulmonary emphysema and fibrosis. Tissue stain positive for acid-fast bacilli, cultures and guinea pig inoculation negative.

of the structural units of the lung tissue in the form of focal emphysema, blebs, bullae or bullous cysts, bronchiolar obliteration or ectasia, and atelectasis of diseased areas. The characteristic x-ray film features are illustrated on roentgenograms of cavities prior to effective chemotherapy and resultant open lesions, correlated with bacteriology and pathology, in two patients (Figures 1 and 2). Six patients died. Autopsy showed that advanced cavitary tuberculosis had contributed to pulmonary emphysema and fibrosis, which led to impairment in pulmonary circulation and cor pulmonale, but was not the immediate cause of death, in five cases. The sixth died of complications following abdominal surgery (see Fig. 1).

General Comments

The recovery of tubercle bacilli in four of our patients, on single cultures only, after periods of up to 76 months of bacteriologic remission, and the finding of acid-fast organisms on tissue stain in two of these patients, which could not be cultured and were not infectious for guinea pigs eight and nine months later on continuous chemotherapy seems significant. In our experience, the persistent "air space"-containing defect due to necrotizing tuberculosis may represent completely or partially healed cavity, or residuals of a previous cavity, in the form of emphysematous bullae or cystic-like lesions, as reported by clinicians, radiologists and pathologists.

The writers would like to stress the truism of the role of the so-called "resistance factors," intrinsic and extrinsic, genetic and immunologic, of the individual patient in the dynamics drug-tubercle bacillus-host relationships that may explain why some patients with tuberculous cavities, with comparable lesions and chemotherapy, reached the status of "open negative" and others remained "therapeutic failures."

It may be of interest to point out that many patients in this series showed marked improvement in their mental states. It has been our experience that inactivation or removal of tuberculous lesions in neuropsychiatric-tuberculosis patients have contributed to a dramatically improved neuro-psychiatric condition in the majority of patients.

Discussion

Reviewing the literature pertaining to the phenomenon, it is apparent that anatomic open-healing of tuberculous cavities has been known to occur, though very rarely, prior to the discovery and use of effective antituberculosis drugs. The mechanisms of anatomic open-healing has been well documented and resultant forms of "open negative" tuberculous cavity reported by pathologists, thoracic surgeons, and research workers on animals. W. R. Webb and associates in their recently published report[7] on 200 resections of tuberculous cavities between 1955 and June, 1959 in 188 patients, with at least two months of bacteriologic negativity and x-ray stability, demonstrated acid-fast organisms on tissue stain, culture, or both in 42.5 per cent of resected specimens. In earlier clinical publications[8-11] the high rate of relapses during the next five years, circa 40 per cent, in patients with non-resected "open negative" tuberculous cavities has been emphasized and it has been stressed that in similar cases with resected cavities only 9 per cent of patients relapsed. The new concept of chemotherapy used over prolonged periods of three to five years or continuously in patients with non-resected "open negative" syndrome improved the early results and lowered the relapse rate to approximately 8.8 per cent.[12-17] The reported evaluation of our study forms the basis for our opinion that effective, continuous chemotherapy seems to be indicated for patients with non-resected open tuberculous lesions and perhaps is to be preferred to extensive excisional procedures for patients who are poor surgical risks. We feel that these patients, after 12 months of bacteriologic remission under coverage of chemotherapy, may be classified as probably inactive and discharged from the hospital.

SUMMARY

Thirty neuropsychiatric-tuberculous patients with "open negative" tuberculous cavities have been closely followed from two to over ten years. They have been treated by individualized combined chemotherapy from two to six years, depending on the extent of disease and patients' response to treatment. After two to five years of bacteriologic remission and x-ray film stability the patients received INH alone, 300 mg. daily. Four had single positive cultures after periods of up to 76 months of bacteriologic negativity with no x-ray shadow worsening.

Radiologic results reflecting changing morphology of lesions which followed prolonged sterilizing chemotherapy may explain the difficulties in interpretation of x-ray

findings and discrepancies between roentgenograms and morphology found on pathologic examination.

The reported data form the basis for the writers' opinion that effective, prolonged chemotherapy seems indicated in patients with non-resected "open lesions" and that these patients, after 12 months of bacteriologic remission under chemotherapy, might be classified as probably inactive. INH, 300 mg. daily, given after 24 months of bacteriologic negativity has proved effective in preventing relapses.

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RESUMEN

Se han observado estrechamente treinta enfermos neuro-psiquiatricos tuberculosos con cavernas tuberculosas "abiertas negativas" siguiéndolos durante dos a diez años. Se han tratado con quimioterapia combinada individualizada de dos a seis años dependiendo de la extensión de la enfermedad y de su respuesta al tratamiento. Después de dos a cinco años de remisión bacteriológica y de estabilización los enfermos recibieron INH solamente a la dosis de 300 mg. por día. Cuatro tuvieron cultivos positivos aislados despues de periodes hasta de 76 meses de negatividad sin empeoramiento radiológico.

Los resultados radiológicos que señalaron cambios en la morfología de las lesiones que siguieron a una prolongada quimioterapia pueden explicar las dificultad de interpretación de los hallazgos radiológicos y las discrepancias entre las radiografías y la morfología encontrada al exámen anatomopatológico.

Los datos referidos consituyen las bases para la opinión de los autores de que la terapéutica efectiva prolongada parece indicada en los enfermos con lesiones no resecadas "curadas abiertas" y que estos enfermos, despues de 12 meses de remisión bacteriológica bajo quimioterapia podrían ser clasificados como probables inactivos.

La dosis de 300 mg. de INH durante 24 meses de negativación bacteriológica se ha mostrado efectiva para evitar recaidas.

RESUMÉ

30 malades tuberculeux d'un service de neuropsychiatrie atteints de cavernes tuberculeuses évolutives, sans expectoration bacillifère ont été étroitement suivis pendant une période s'étendant de deux à dix ans. Ils ont été soumis à un traitement associé variant selon chaque cas, pendant une période de deux à six ans, dépendant de l'étendue de la maladie et de la réponse du malade au traitement. Après deux à cinq ans de rémission bactériologique, et de stabilité radiologique, les malades reçurent de l'isoniazide seul, à la dose de 300 mmg. par jour. Quatre d'entre eux eurent une seule culture positive après des périodes allant jusqu'à 76 mois de négativité bactériologique, et sans aggravation de l'opacitè radiologique.

Les résultats radiologiques reflétant les modifications de la morphologie des lésions qui suivirent une chimiothérapie stérilisante prolongée peuvent expliquer les difficultés d'interprétation des constatations radiologiques, et les divergences entre les clichés et les constatations faites á l'examen anatomo-pathologique.

Les faits rapportés constituent le fondement de l'opinion des auteurs, pour lesquels une chimiothérapie efficace, prolongée, semble indiquée chez les malades atteints de lésions évolutives non opérées, et que ces malades, après douze mois de rémission bactériologique sous chimiothérapie, peuvent être classés comme probablement inactifs. L'isoniazide, á la dose de 300 mmg. par jour, donné après 24 mois de négativité bactériologique a prouvé son efficacité dans la prévention des rechutes.

ZUSAMMENFASSUUNG

30 Geisteskranke-Tuberkulöse mit "offen negativer" tuberkulösen Kavernen wurden 2 bis mehr als 10 Jahre lang sehr genau verfolgt. Sie wurden behandelt mit individuell kombinierter Chemotherapie während 2 - 6 Jahren je nach der Ausdehnung der Erkrankung und der Reaktion des Patienten auf die Behandlung. Nach 2 - 5 Jahren bakteriologischer Besserung und röntgenologischer Stabilisierung erhalten die Patienten ausschliesslich 300 mg. INH täglich. 4 Kranke hatten vereinzelt positive Kulturen von bis zu 76 Monaten bakteriologischer Bazillenfreiheit und ohne Verschlechterung der röntgenologischen Verschattungen.

Die röntgenologischen Ergebnisse, indem sie dem Wandel in der Morphologie der Herde wiedergeben, wie er auf eine sehr lange Zeit durchgeführte sterilisierende Chemotherapie folgt, können die Schwierigkeiten in der Interpretation der Röntgenbefunde und die Diskrepanzen zwischen Röntgenaufnahmen und der bei der pathologischen-nanatomischen Untersuchung zu findenden morphologischen Verhältnisse erklären.

Die aufgeführten Befunde stellen die Grundlage dar für Auffassung des Autors, wonach eine wirksame und lange fortgesetzte Chemotherapie indiziert erscheint bei Kranken mit nicht resezierten "offenen Herden" und daß diese Patienten nach 12 Monaten bakteriologischer Besserung unter der Chemotherapie doch als wahrscheinlich inaktiv klassifiziert werden können. INH 300 mg. Täglich 24 Monate nach bakteriologisch erreichter Bazillen freiheit haben sich als wirksam erwiesen zur Verhütung von Rückfällen.

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The Treatment of Regurgitant Esophagitis by Reconstruction of the Cardiac Sphincter Mechanism in Patients with No Demonstrable Hiatal Hernia*

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Introduction

Since esophagitis was first described in 1879 by Quinke,[1] a number of papers based on clinical and laboratory observations have been published associating esophagitis with the regurgitation of acid-peptic juice from the stomach.[2-5] Although Jackson[6] described peptic ulcers of the esophagus in 1927, Winklestein[7] is usually given the credit for first describing peptic esophagitis as a new clinical entity in 1935. He stated that the mechanism of its production was not entirely clear. In 1957, he[8] discussed peptic esophagitis associated with duodenal ulcer, and suggested it as part of the ulcer diathesis as is the duodenitis and antral gastritis seen in association with a peptic ulcer. Since many patients with severe ulcer diathesis have no associated esophagitis, and since other patients with a known gastric hypoacidity may develop severe esophagitis, this is not the only explanation for the production of such esophageal changes. Whether an ulcer diathesis exists or not, the transcardial reflux of gastric juice into the lower esophagus is the *sine qua non* in the development of the esophagitis. In the absence of such abetting factors as prolonged severe vomiting, the presence of a nasogastric tube, or surgery on the esophagogastric junction, regurgitant esophagitis is most likely due to an incompetent cardiac sphincter mechanism associated with a hiatal hernia. It is the general experience that a hiatal hernia can be demonstrated in 70 to 85 per cent of individuals with proved esophagitis.[9,10] Hiatal hernias are frequently missed on routine upper gastrointestinal studies, however, and small hernias may be difficult to demonstrate even when special efforts are made (Fig. 1). In a recent review of 130 patients with esophagitis, 103 of whom had a hiatal hernia, the hernia was found in six patients only after repeated x-ray examinations.[9] Maurer[11] has stated that only 60 per cent of hernias of the esophageal hiatus will be demonstrated on the first x-ray examination. Although no hernia is found, the fluoroscopist may be able to demonstrate free regurgitation of barium from the stomach into the lower esophagus that indicates an incompetency of the cardiac sphincter mechanism to account for the patient's esophagitis. One can conclude from such facts that what otherwise might be referred to as a primary esophagitis, unassociated with specific abetting factors, is actually in many instances esophagitis secondary to a small unrecognized hiatal hernia. Moreover, if a small "traction" hernia is seen, it is more likely the cause than the result of the coexisting esophagitis. In view of such considerations, as well as the known satisfactory results in treating esophagitis by repair of an associated hiatal hernia, it is fair to assume that certain patients with proved chronic

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esophagitis and no other specific abetting factor will benefit by reconstruction of the cardiac sphincter mechanism even though no definite hernia is demonstrated by roentgenographic techniques.

The present report is based on eight patients with chronic acid-peptic esophagitis in whom no hiatal hernia was demonstrated by x-ray studies. All eight patients were operated upon and had the cardiac sphincter mechanism reconstructed as in the usual hiatal hernia repair described by Allison.[4] Utilizing a transthoracic approach, the stomach and esophagus are dissected from their attachments in the region of the esophageal hiatus. A counter incision is made in the diaphragm. An umbilical tape previously placed around the esophagus is passed through the hiatus and back out the counter incision to place traction on the esophago-gastric junction, and to maintain it below the diaphragm during the repair. The hiatus is reconstructed by approximating the two limbs of the right crus behind the esophagus with interrupted sutures. The new hiatus should permit the comfortable admission of the forefinger. The pharyngo-esophageal ligament is repaired by suturing the esophagus circumferentially to the new hiatus. The fundus of the stomach is then sutured to the under surface of the diaphragm through the counter incision to help maintain the acute angle of entry of the esophagus into the stomach. The counter incision is closed to complete the repair. In this manner, the structures making up the cardiac sphincter mechanism are reconstituted, and the further regurgitation of acid-peptic juice is prevented. There were six men and two women ranging in age from 35 to 49 years. The presence of esophagitis was confirmed pre-operatively in all patients by means of esophagoscopy. The changes seen ranged from reddening and edema of the esophageal mucosa in its terminal portion to actual linear

FIGURE 1: Two upper gastrointestinal studies a year apart on a patient with severe symptoms of esophagitis. (A) No evidence of a lesion reported. (B) A large hiatal hernia seen. The presence of esophagitis was confirmed on each occasion by esophagoscopy. In the interval between the two studies, she failed to respond to medical therapy for the esophagitis; has been asymptomatic since repair of the hernia. The need for repeated examinations for a hiatal hernia coexisting with esophagitis resistent to medical therapy is obvious.

erosions and ulcerations with associated bleeding. Medical therapy consisting of an ulcer diet, antacids, and elevation of the head of the bed had been tried for varying periods of time by the referring physician and was found to be unsuccessful before surgery was considered.

Case Reports

Case 1: M. B., a 37 year-old white laboratory worker who had the onset of epigastric and substernal pain 14 years prior to admission. The burning pain was aggravated by drinking alcoholic beverages, dietary indiscretion, smoking, and lying down after meals. The pain was partially controlled for short intervals by diet and antacids. X-ray films failed to show evidence of the presence of an esophageal hiatal hernia. The physical examination was not remarkable. On December 12, 1958, an esophagoscopy was done which revealed mild chronic esophagitis with free regurgitation of gastric juice into the terminal esophagus. Following this examination, reconstitution of the cardiac sphincter mechanism was done through a transthoracic approach. At the time of surgery, the esophageal hiatus was slightly patulous and no evidence of a hiatal hernia was seen. His postoperative course was uneventful with discharge from the hospital on the ninth postoperative day. He returned to work two weeks later, and has been entirely asymptomatic to the present time on an unlimited diet containing foods that could not be ingested previously.

Case 2: E. D., a 35 year-old white steel worker was admitted complaining of substernal burning of four years duration aggravated by lying down after meals and at night. He had been on ulcer therapy with little relief for the first two years of his illness, but he discontinued this therapy when he realized it was not helping. Upper gastrointestinal studies done at that time showed no evidence of a hiatal hernia, gastric, or duodenal ulcer. On two prior hospital admissions he had been esophagoscoped, and severe esophagitis with ulceration was noted in the terminal esophagus. He entered the hospital for surgery complaining of an increase in his symptoms for the prior three months. Physical examination was non-contributory. X-ray examination again failed to demonstrate a hiatal hernia. He was again esophagoscoped and minimal esophagitis with regurgitation of gastric juice was demonstrated. He returned to the hospital two months later for surgery which was done on April 22, 1957. At the time of surgery it was noted that there was slight bulging of the stomach through the diaphragm. His postoperative course was uneventful except for a hydrothorax on the left which cleared with a single aspiration. Discharge from the hospital was on the 13th postoperative day. He has been asymptomatic to the present time except for occasional chest wall pain.

Case 3: A. H., a 35 year-old white salesman was admitted to the hospital with a nine month history of substernal distress and postprandial pain, particularly aggravated by alcoholic intake which was seemingly a necessary part of his job. Physical examination was non-contributory. On March 24, 1956, he was esophagoscoped. A moderate esophagitis with linear erosions was noted. X-ray examinations showed no evidence of an associated hiatal hernia. He was placed on the usual medical regimen with no satisfactory relief of his symptoms, and he returned to the hospital for surgery on May 28, 1956. At the time of surgery a small, but definite hernia was seen. The postoperative course was satisfactory, and he was discharged from the hospital on the 13th postoperative day with complete relief of his symptoms. He has returned to his prior occupation as a salesman with no recurrence of symptoms.

Case 4: M. M., a 38 year-old white housewife complained of a seven-month history of epigastric and precordial pain with associated bloating. The pain was occasionally associated with meals. There was no increase in the pain when the patient lay down, and there was partial amelioration of the symptoms by antacid therapy. Physical examination and the laboratory findings were non-contributory. An upper gastrointestinal series was done which was reported as normal. The electrocardiogram was likewise normal. On March 25, 1955, she was esophagoscoped and a hiatal hernia repair done. A minimal esophagitis was seen on esophagoscopy. At the time of the repair, a small herniation of the stomach into the chest was noted. Her postoperative course was uneventful, and she has remained asymptomatic since the operation.

Case 5: C. C., a 46 year-old white man was first admitted to the hospital on April 29, 1956 with the chief complaint of a "pinched esophagus." He gave the history of about nine months of dysphagia, stating that food would catch just before entering the stomach. He likewise had burning substernal pain. A diagnosis of esophagitis was made, and he was placed on a medical regimen consisting of antacids and an ulcer diet without relief. He was admitted to the hospital again on May 28, 1956 with similar complaints of epigastric pain associated with regurgitation of food after eating. There was some relief of this substernal pain by antacids, although the pain was gradually increasing in severity. He again complained of food sticking in the lower esophagus. Physical examination and laboratory studies were non-contributory. The electrocardiogram was normal on this admission. X-ray examination of the upper gastrointestinal tract showed normal emptying of the esophagus with no evidence of a hiatal hernia. Esophagoscopy was done, and edema and reddening of the mucosa of the terminal esophagus was seen with definite regurgitation of gastric contents into

the lower esophagus. Because of the prolonged history and the esophagitis demonstrated by esophagoscopy, reconstruction of the cardiac sphincter mechanism was done. Although no definite herniation was seen, there was some enlargement of the esophageal hiatus that could permit herniation of the stomach into the chest under the proper circumstances. Postoperatively he did well, and he has had complete amelioration of his preoperative symptoms.

Case 6: C. C., a 49 year-old white man was first admitted to the hospital on April 7, 1957, with the chief complaint of heart burn and retrosternal pain. He gave a three-year history of heart burn after meals, especially after those consisting of greasy foods. At times, this pain was extremely severe, and it was occasionally associated with dysphagia. Physical examination and laboratory studies were non-contributory. The patient was esophagoscoped on this admission, and the esophagoscopy was reported as normal. An upper gastrointestinal series failed to demonstrate the presence of a hiatal hernia. Because of the extreme symptoms of esophagitis over a long period of time, a hiatal hernia repair was done. At the time of surgery, a definite small hiatal hernia was noted. Following the usual hernia repair, the patient did well postoperatively, and he is no longer troubled by his preoperative symptoms.

Case 7: R. R., a 39 year-old white engineer entered the hospital on June 2, 1959 with a history of epigastric pain, substernal burning, and a one-year history of occasional melena. His pain was aggravated by highly seasoned foods and relieved by milk. Physical examination and laboratory studies were non-contributory. X-ray films taken one and one half years prior to this admission demonstrated a mild deformity of the duodenal bulb, but those taken on the present admission showed no such abnormality. Likewise, there was no abnormality of the esophagus reported, nor was a hiatal hernia demonstrated. Esophagoscopy was done which revealed a minimal to moderate esophagitis and the presence of a small hernia. Although the esophagitis was not severe, it appeared to be chronic in nature in that there were hyperplastic changes of the esophageal mucous membrane present. Reconstruction of the cardiac sphincter mechanism was done through a transthoracic approach. The esophageal hiatus was somewhat more patulous than normal although the changes were minimal. No evidence of hernia was noted. His postoperative course was uneventful, and he was discharged from the hospital on the ninth postoperative day. He soon resumed normal activities completely free from preoperative symptoms in spite of a rather varied dietary intake consisting of highly seasoned and other ordinarily aggravating foods.

Case 8: C. M., a 45 year-old negro housewife had been followed in the hospital dispensary for many years with bronchial asthma. In addition, she had a 12-year history of occasional right upper quadrant and epigastric burning pain made worse by coffee and fatty foods. Repeated x-ray studies of the esophagus, stomach, and gallbladder were interpreted as normal. She was treated intermittently with antacids and antispasmodics with some relief of the pain. An x-ray examination in December, 1958 showed a normal esophagus with no evidence of hernia. A diverticulum of the third portion of the duodenum was demonstrated. She was admitted to the hospital in February, 1959 for further study. Physical examination and laboratory studies were non-contributory. Hyperemia and erosions of the terminal esophagus were seen at esophagoscopy. On March 3, 1959, she was operated upon and her cardiac sphincter mechanism was reconstituted as in hiatal hernia repair. At the time of surgery, an enlarged esophageal hiatus was noted, but no definite herniation of the stomach into the chest was seen. She was discharged from the hospital shortly thereafter, and has been asymptomatic to the present time except for some mild dysphagia which lasted for about two weeks in the immediate postoperative period.

Results

It was possible to observe anatomical changes related to the esophageal hiatus in all patients during the surgical procedure. In five, a small herniation of the stomach into the chest was seen indicating the presence of a small hernia that had not been demonstrated by x-ray. No hernia was seen in the other three patients. The esophageal hiatus was judged to be more patulous than normal. In spite of these minimal changes, all the patients have benefited from the surgical reconstitution of the cardiac sphincter mechanism with complete alleviation of the preoperative symptoms, even on an unrestricted diet. The postoperative period of observation has varied in the individual case from ten months to four years.

Discussion

Inhibition of the damaging effects of acid-peptic juice on the involved esophageal mucosa is the obvious goal of all therapeutic measures in the treatment of reflux esophagitis. Whether this can be accomplished by medical or surgical means is dic-

tated to a great extent by the contribution of associated factors in the development of the esophagitis. Among these are an associated duodenal ulcer, the presence of a hiatal hernia, previous surgery on the esophago-gastric junction, or a bout of severe vomiting. Whereas medical therapy has been generally unsatisfactory in our experience in the treatment of chronic esophagitis with coexisting hiatal hernia, most patients can be helped by the repair of the hernia.[9] In considering the problem of esophagitis, it must be kept in mind continually that a small hiatal hernia can exist in spite of negative x-ray evidence, that this hernia can be the basis for the symptoms and objective findings of the esophagitis, and that repair of such an unrecognized hernia in selected individuals can result in complete amelioration of the patient's preoperative symptoms. The good results in eight patients with a long history of proved esophagitis, but no demonstrable hiatal hernia, who were treated in this manner after failure to respond to acceptable medical therapy strengthens this contention.

SUMMARY

1. The relationship of insufficiency of the cardiac sphincter mechanism and regurgitant esophagitis is discussed.
2. Surgical reconstitution of the cardiac sphincter mechanism as in hiatal hernia repair is suggested as proper therapy in selected individuals even though no hiatal hernia is demonstrated by x-ray.
3. Case reports of eight patients treated in this manner with good results are given.

RESUMEN

1. Se discurre sobre la relación existente entre la insuficiencia del esfinter del cardias y las esofagitis con regurgitación.
2. La reconstrucción quirúrgica del mecanismo del cardias como en lahernia hiatal se sugiere como tratamiento adecuado en individuos escogidos aunque no se haya demostrado hernia hital a los rayos X.
3. Se presentan las historias de ocho enfermos tratados de este modo con buenos resultados.

RESUMÉ

1. L'auteur discute les rapports de l'insuffisance du sphincter cardiaque et de la régurgitation oesophagienne.
2. Une reconstitution chirurgicale du sphincter cardiaque, comme s'il s'agissait d'une hernie hiatale, est évoquée comme traitement approprié chez des sujets bien choisis, même si aucune hernie hiatale n'est démontrée par l'examen radiologique.
3. L'auteur expose les observations de 8 malades traités de cette façon avec de bons résultats.

ZUSAMMENFASSUNG

1. Diskussion über die Bezeihung der Insuffizienz des Cardia-Sphincter-Mechanismus und der Ösophagitis mit Brechbewegung.
2. Eine chirurgische Wiederherstellung des Cardia-Sphincter-Mechanismus, sowie bei der Behebung der Hiatus-Hernie wird vorgeschlagen als geeignete Therapie bei ausgewählten Fällen auch dann, wenn eine Hiatus-Hernie röntgenologisch nicht nachweisbar ist.
3. Es werden Krankengeschichten wiedergegeben von 8 Patienten, die auf diese Weise und mit guten Resultaten behandelt worden sind.

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Pulmonary Cryptococcosis*

Report of a Case Treated with Amphotericin B

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Since the discovery of amphotericin B, several reports have indicated that it is an effective agent in the treatment of cryptococcosis.[1,2,4,5] A search of the English literature failed to reveal a case of pulmonary cryptococcosis treated with amphotericin B. Kuykendall, *et al.*[3] in 1957, collected from the literature 27 cases of cryptococcosis limited to the lungs and treated by pulmonary resection. To these they added four cases. It was their opinion that pulmonary cryptococcosis should be treated much like malignancy which might metastasize, if not extirpated. However, three of these 27 resected cases subsequently died of cryptococcal meningitis, and follow-up reports of two years or longer are available on only five others.

The portal of entry of Cryptococcus into the body remains obscure, but it is probable that, like histoplasmosis and coccidioidomycosis, the usual entry is through the lung from which dissemination then occurs. The frequency of dissemination from pulmonary disease is not known. Until it is proved that the lung is not the portal of entry and that dissemination to the nervous system occurs from some source other than a primary site in the lung, early and vigorous therapy of pulmonary lesions should be undertaken, because of the unfavorable prognosis once the central nervous system is involved. Prior to amphotericin B, no chemotherapeutic agent had been discovered which was of unquestioned value in the treatment of this disease. The present report demonstrates the apparent effectiveness of amphotericin B in a pulmonary cryptococcosis patient in whom resection could not be carried out because of involvement of both lungs.

Case Report

N. L. is a 33 year-old white clerical worker who was in excellent health until August 27, 1957, when he fractured his right middle finger while playing softball. He was hospitalized and a routine chest x-ray film showed 1.5 cm. oval density in the infraclavicular portion of the left lung field at the level of the second anterior intercostal space and another smaller oval density on the right near the end of the second rib (Figure 1). The possibility of granulomata or metastatic cancer was considered. The white blood cell count was 6,850 per cubic mm. with 74 per cent neutrophils and 26 per cent lymphocytes. The hemoglobin was 12.9 grams per 100 ml. and the erythrocyte sedimentation rate was 10 mm. per hour (Wintrobe method). A search for a primary site of a possible malignancy was made, but gastrointestinal series, barium enema, and intravenous pyelograms were negative. Bronchoscopy was normal. A culture of bronchial secretions, aspirated at the time of bronchoscopy was negative. He was discharged and continued to work until December 2, 1957, when he returned to the hospital with complaints of dry cough, chest pain, and weakness for 10 days. A

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**Resident in Medicine. The contents of this article are the personal views of the Air Force author and are not to be construed as statement of official Air Force policy.

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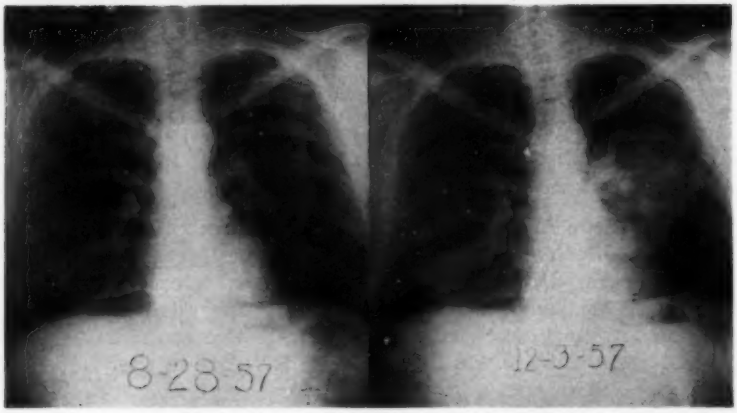

FIGURE 1 FIGURE 2

FIGURE 1: Chest x-ray film dated August 28, 1957 showing a light patchy infiltrate in the second anterior interspace on the left, and a smaller round density near the end of the second rib on the right. FIGURE 2: Chest x-ray film dated December 3, 1957, showing multiple large and small nodular densities bilaterally and diffuse hazy infiltrate in the left mid-lung field.

chest x-ray film at this time revealed multiple large and small nodular densities bilaterally (Figure 2). A bone survey was negative. At this time the white blood count was 5,300 per cu. mm. with 57 per cent neutrophils and 31 per cent lymphocytes, 11 per cent monocytes and 1 per cent eosinophils. The hemoglobin was 13.4 gm. per 100 ml. and the sedimentation rate was 34 mm. per hour. A bone marrow aspiration revealed no malignant cells. Bronchoscopy was repeated and was negative. A needle aspiration of one of the lung lesions showed many mononuclear inflammatory cells.

He was transferred to the Veterans Administration Hospital in Oklahoma City, Oklahoma with no additional symptom except a 10 pound weight loss. The physical examination at this time revealed a well developed, well nourished white man who did not appear ill. There was slight dullness over the base of the left lung with diminished breath sounds in the same region. A biopsy of the right scalene fat pad revealed normal lymphoid tissue without evidence of malignancy or granuloma. The

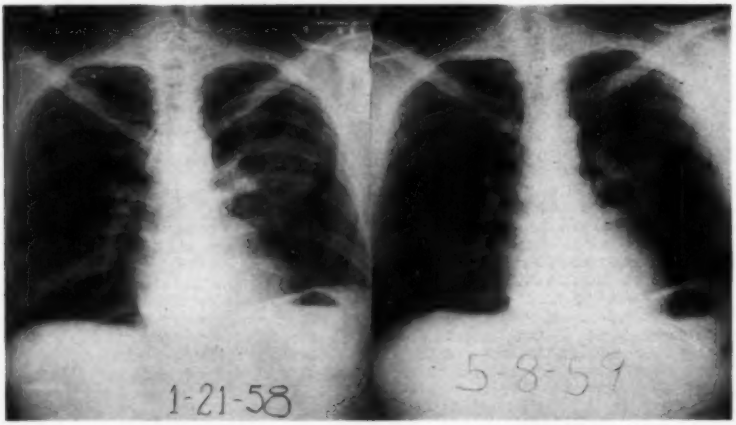

FIGURE 3 FIGURE 4

FIGURE 3: Chest x-ray film dated January 21, 1958, 19 days after thoracotomy. There has been considerable clearing of the infiltrates. FIGURE 4: Chest x-ray film dated May 8, 1959, revealing further clearing, especially of the infiltrate in the left mid-lung field.

skin tests with tuberculin, coccidioidin, and blastomycin were negative. On January 2, 1958, he underwent exploratory thoracotomy. A frozen section of the lesion from the superior segment of the lower lobe of the left lung suggested granuloma. A yeast-like organism was seen in the hematoxylin-eosin preparations. A culture of the biopsy specimen grew out *Cryptococcus neoformans*. The chest x-ray film 19 days after operation showed considerable clearing of the infiltrates (Figure 3). Examination and cultures of the cerebro-spinal fluid were negative.

Amphotericin B* susceptibility studies by a modified tube dilution method[6] on this strain of Cryptococcus showed *in vitro* inhibition at a concentration of 0.047 mcg./ml. Preliminary metabolic studies on this organism in the Warburg apparatus showed that amphotericin B depressed oxygen uptake proportional to the concentration used with an effect note dat levels as low as 1.0 mcg./ml.[7]

On February 4, 1958, he was begun on intravenous amphotericin B and this therapy was continued daily until Aprii 8, 1958, when he was discharged from the hospital free of symptoms. The total dose of the drug was 2700 milligrams. Figure 5 summarizes his treatment with amphotericin B. The pertinent laboratory values are also shown. Since his discharge, he has worked at his job as clerk in an office and has required no time off for illness. His weight in December, 1957, was 171 pounds and when last seen May 8, 1959, it was 185 pounds. The chest x-ray film on May 8, 1959 revealed further clearing and shrinking of the infiltrate on the left with virtual disappearance of the lesions on the right (Figure 4).

Discussion

During amphotericin B therapy, the patient exhibited a mild febrile response with chills. This response usually occurred on the day the dosage was increased, and was not noted during the time he was receiving 50 mgm. daily. The febrile response and the azotemia are the best known side reactions of the drug and only rarely necessitate the discontinuance of the drug. In subsequent patients we have treated with amphotericin B, the immediate reactions, but not the azotemia, have been minimized with the use of chlorpheniramine and other drugs of the antihistamine and tranquilizer groups. It is interesting that the hemoglobin of the patient declined during therapy and returned to normal after the drug was discontinued. Unfortunately the stools were not examined for occult blood. Seabury and Dascomb[4] found extensive intestinal ulceration in one of 18 patients treated with amphotericin B and another patient had significant melena. It is possible that the decrease in hemoglobin may have been due to occult gastrointestinal bleeding although intestinal complaints were not present in the patient. We have observed the development of mild normochromic, normocytic anemia in other patients receiving amphotericin B and this is currently being investigated. Slight elevation in the retention of bromsulphalein also occurred in this patient.

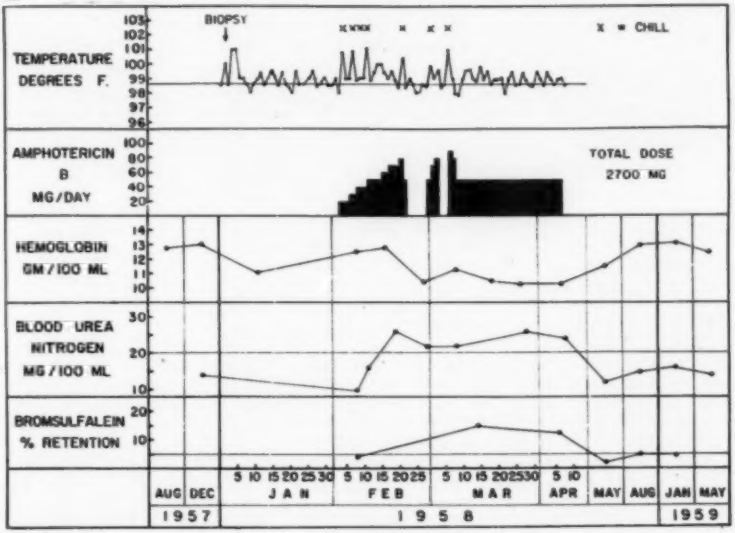

FIGURE 5

*Fungizone (E. R. Squibb and Sons, Division of Olin Mathieson Chemical Corp.)

Caution must be used in ascribing a beneficial effect to any form of therapy in this disease in view of the characteristic chronic course with remissions and exacerbations. In the case reported here, the weight gain, feeling of well-being, and change in the x-ray film appearance of the lung lesion seem to be due to a beneficial influence of amphotericin B. However, the evaluation of the patient's response is complicated by some improvement in the x-ray film appearance of the lung lesions before drug therapy was instituted.

Present knowledge of human cryptococcosis indicates that surgical excision of pulmonary lesions offers the best opportunity for cure.[3,5] Amphotericin B should be used when bilateral disease or other factors prohibit surgical resection of pulmonary lesions. Surgical excision combined with chemotherapy should be advantageous for those patients in whom resection can be carried out.

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THE ELEVATOR ESOPHAGUS

The authors present a vivid description of bizarre esophageal motility. It is recognized on fluoroscopic examination, with the aid of contrast medium, with the patient in the erect position. A swallow of barium remains in the esophagus for several minutes, intermittently rising from the lower esophagus to the level of the aortic arch with moderate speed and then falling back again. Occasionally the barium column bounds rapidly almost to the hypopharynx. This erratic motion resembles that of an elevator gone wild.

Twenty cases have been presented in 18 of which erratic esophageal motility was a clue to the presence of disease. Nine patients had some form of malignant tumor. They believe that the elevator phenomenon is a reflection of physiologic dysfunction of the lower esophagus and a lesion in or near the lower esophagus may be the trigger mechanism which disturbs normal neuromuscular function. This seems to be borne out by follow-up of the four patients who have had surgical or radiation treatment of an obvious lesion in this area. They are now symptom-free and without demonstrable erratic esophageal activity, although in two there is known residual malignant disease elsewhere.

The condition described may simulate the clinical picture of cardiospasm, but the fluoroscopic findings are different and their patients have neither a positive Mecholyl test nor the fixed contraction deformity of cardiospasm. There is a similarity to the Barsony-Teschendorff syndrome or segmental esophageal spasm, except that the substernal pain is less severe and none of their patients has shown the pronounced segmental contractions or "pearl-necklace" appearance of barium in the esophagus.

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Pulmonary Atelectasis Due to Voluntary Suppression of Cough*

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Massive pulmonary atelectasis is encountered in a variety of circumstances that predispose to, or produce bronchial obstruction. The obstructing agents may be tumors, intrinsic or extrinsic, foreign bodies, or abnormal secretions retained in the airways. Precipitating factors may be inhibition of the cough mechanism by drug or metabolic depression, reflex inhibition due to pain, or ineffective motion due to interrupted integrity of the chest wall, to name but a few.

An additional factor, not as a rule noted, may be voluntary suppression of cough, such as was observed in the five cases to be presented here. Emotional motivation toward suppression of cough was present in at least four of the five; repeated bronchoscopic examination and explorations ruled out intrinsic disease of the airways, and four of the five patients had recurrences of the atelectatic phenomenon until they ceased to suppress their cough mechanism.

The importance of cough, unique in its capacity to accelerate expiratory air flow is indicated by the studies of Ross *et al.* and the particular importance of cough in preventing atelectasis has been demonstrated by Dayman and Manning.

Case 1 presented at the age of 23 with massive atelectasis of the right lower lobe. The x-ray film (Fig. 1a) is classical. Bronchoscopy disclosed thick, airless mucoid secretions completely filling the lower lobe bronchus on the right. This was aspirated and partial re-expansion was noted immediately (Fig. 1b), followed shortly by complete re-expansion. However, the condition recurred several times during ensuing months until it was discovered that this person considered a cough as a social handicap and therefore had learned to suppress it completely; this in spite of an almost continuous allergic mucoid secretion. The problem of recurring atelectasis was solved when it was impressed on the patient that coughing was less of a social handicap than recurring atelectasis.

FIGURE 1a FIGURE 1b

FIGURE 1a: Atelectasis of the right lower lobe. FIGURE 1b: Partial re-expansion directly following bronchoscopy.

*Presented at the 25th Anniversary Homecoming Meeting, American College of Chest Physicians, Albuquerque, New Mexico, October, 1959.

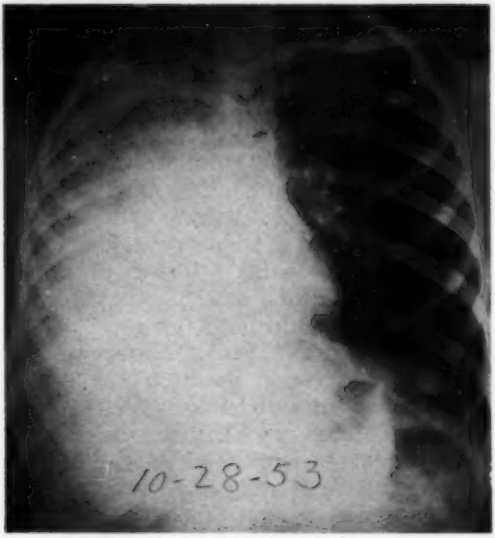

FIGURE 2: Atelectasis of right lung.

Case 2 was a girl of eight years. She was asthmatic and had learned to suppress her cough reflex in order to avoid annoying her parents. On October 28, 1953 (Fig. 2) she exhibited atelectasis of the right lung. This responded to bronchoscopy, but was followed immediately by atelectasis of the right lower lobe. A second bronchoscopy November 1, 1953 together with measures to liquefy secretions, failed to secure complete re-expansion and on November 22, atelectasis of the right upper lobe was found. The voluntary suppression of cough was then noted and measures were taken to encourage cough and expectoration. During the next few months, the condition recurred several times, but finally responded to conservative measures as well as permissive encouragement on the part of the parents for her to cough freely.

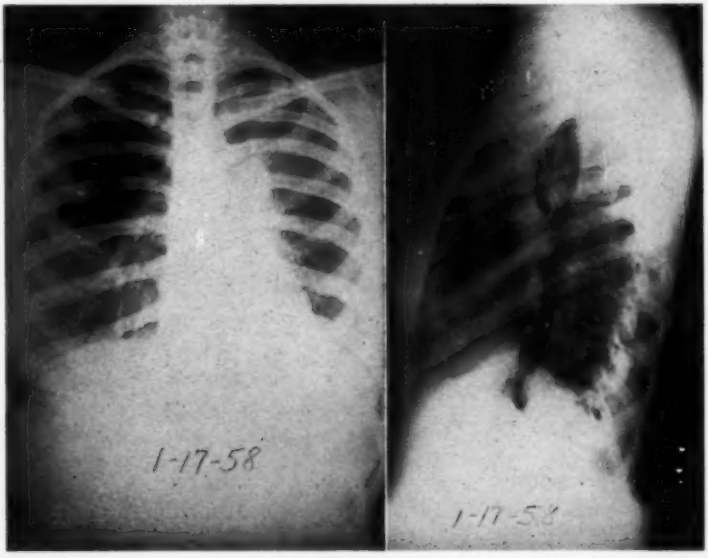

FIGURE 3: Pulmonary atelectasis of left upper lobe. In the lateral view, the interlobar fissure can be seen to be displaced upward and forward

Case 3 was a girl 16 years of age, the younger of two sisters. The older one was asthmatic with a chronic cough that was a source of irritation to her family. The younger sister proudly announced that she did not need to cough even when she had a cold. When examined on January 17, 1958 she was dyspneic and had the classical physical and x-ray film findings of atelectasis of the upper lobe of the left lung (Fig. 3). Bronchoscopy disclosed this lobar orifice to be completely obstructed by inspissated mucopus with a putty-like consistency. This was removed with a foreign body forceps, whereupon there was almost complete re-expansion in the next hour. As far as is known, she never had a recurrence.

Case 4 was a strikingly beautiful young woman who had a mildly suppurating bronchiectasis involving the left lower lobe. In social and business contacts, she had learned to suppress her cough most effectively. She suffered repeated episodes of right chest pain and low grade fever, associated with an atelectatic shadow in the middle lobe area of the right lung. Subsequent experience demonstrated that the episodes of chest pain and fever could be avoided or made less severe by free and uninhibited coughing in order to clear out her bronchial tree.

FIGURE 4: Massive atelectasis of left lung.

Case 5. This 66 year-old woman with no previous respiratory disease presented with massive atelectasis of the left lung (Fig. 4), marked by fever and dyspnea. There was no cough. She had been in a depressed state and was wont to sit quietly for hours at a time. Bronchoscopy disclosed the left main bronchus filled with tenacious mucopus which recurred from the secondary orifices until it had been aspirated several times. The mucosa was red, but showed no other evidence of disease. The atelectasis did not re-expand immediately after bronchoscopy, but did so after a few days, when she was forcibly ambulated. Two weeks later, the identical picture recurred and responded the same way. She was then put on dexedrine, encouraged to cough and had no more episodes of atelectasis.

Discussion

Most people find cough an annoyance, either to have or to hear. It is more than a euphemism to classify it as a protective mechanism, although it may fail to serve much of a purpose, particularly in conditions of acute inflammation. That its suppression, however, may lead to trouble, and that such suppression may voluntary, is suggested by this group of patients.

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A Case Report of Thymic Cyst*

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Advances in diagnostic aids and surgery have made successful extirpation of mediastinal tumors a relatively common experience. With these results, reports of classification of tumors have become more numerous in recent years. However, very little literature has been encountered concerning thymic cysts and in this report our experience is presented where various attempts to overcome the problem of diagnosis were made.

Case Reports

T.I., a man aged 24, clerk, was found to have an abnormal, round, sharply defined shadow in the left hilar region during a routine chest x-ray film examination in November of 1957 (Fig. 1). When he was referred to us, preliminary physical examination revealed no other unusual findings and there was no subjective symptom. No particular picture was presented by his family or past history except that a year and a half prior to this routine examination, he had a chest x-ray film taken in which a slight abnormal outline in the left hilar region was noted. However, no precaution or follow-up examination was deemed necessary at that time and he passed the physical examination of his company.

At this time and during the period of his hospitalization, there was no abnormal finding noted. The brachial blood pressure was 130/80 mm.Hg. and no increase of dullness was noted over the left hilar region. Clinically there was no symptom to suggest thyroid, thymus or circulatory diseases. Radioiodine uptake, urinary 17-ketosteroid values, repeated sputum examinations, E.C.G., W.R. test, hematological findings and blood chemistry were all negative.

In an effort to elucidate the character of the shadow, x-ray kymogram was taken and a pulsation in phase with the heart movement was noted. Owing to its round outline and position, aortic aneurysm was also suspected, but the kymogram readings were not helpful in differentiating this point. Artificial pneumothorax of the left side was then carried out to determine if the tumor had its origin in the parenchyma of the lung and as a preliminary step before thoracoscopy (Fig. 2).

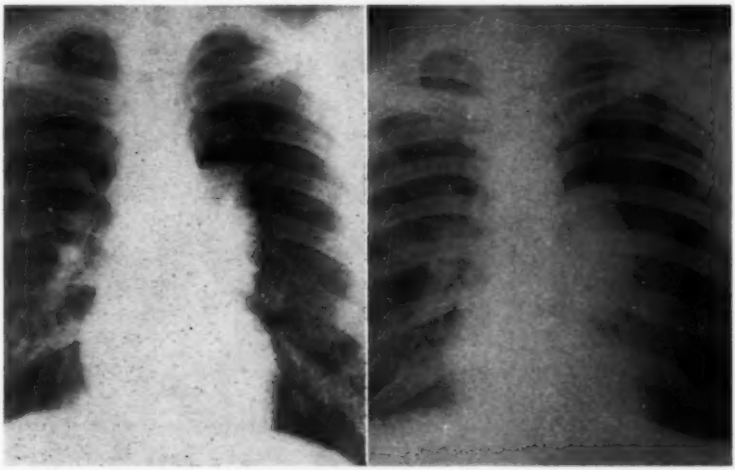

FIGURE 1: At the time of admittance. FIGURE 2: After artificial pneumothorax.

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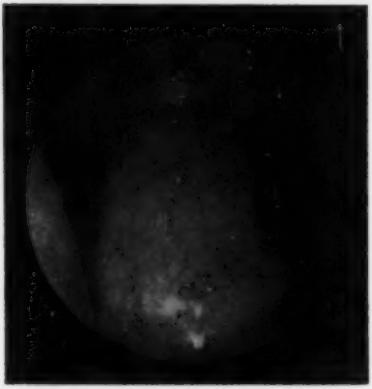

FIGURE 3: Viewed through chest wall with laparoscopic tube.

Bronchography was considered unnecessary after a series of high voltage chest x-ray films were taken.

After careful pneumothorax procedures were carried out, it became clear that the tumor was not that of the lung or the bronchi and that its wall was free from adhesions to the surrounding tissues. Thoracoscopy procedures were taken by using special laparoscope tube and camera of our clinic. Through this procedure, a tumor the size of a small pear was clearly seen moving quite freely in rhythm with the heart beat (Fig. 3).

The surface of the tumor was tense and smooth with rich capillary network, but no adhesion to the lung or pleura was evident and its site was in the anterior mediastinum overlapping the pericardium.

When the left side of the mediastinum was exposed under surgery, the oval tumor was found to be attached to the anterior position just above the atrium and was free of the pleura or the pericardium. The pedicle was located on the elongated side and was detached quite easily. After further exploration of the surrounding parts showed no signs of other growths, the chest was closed. The recovery was uneventful.

FIGURE 4: Gyrus-like formation inside the cyst.

Histopathologic Findings

The tumor was the size of a large lemon and had a thick, tense capsular fibrous wall It was a unilocular cyst containing light brown viscous fluid and some parts of the inner side of the wall showed a brain gyrus-like formation and a polyp-like growth (Fig. 4).

The fibrous tissue of the capsular membrane stained blue and a picture of cholesterin deposits below was seen with tumor growth on its right (Fig. 5). The section showing growth showed diffuse lymphoid cells and between these cells, a medium-sized reticulo-epitheloid cell possessing light chromatin network was evident. The cells were bridged together in netlike formation through protoplasmic protrusions, but had no connection with silver staining fibers when seen with the silver method. It is therefore believed to be a benign lympho-epithelioma of the thymus. Furthermore, in this case, Hassall's bodies could not be found.

Discussion

It is not clear whether the cyst was present in the thymus and later became neoplastic or whether it was lympho-epithelioma from the beginning and later became cystic. However, since the tumor cannot be seen in all parts of the cyst wall and grouping of lymph cells and cholesterin crystals can be seen within the thick fibrous capsular membrane, an interpretation may be made that formerly thymic tissues, especially Hassall's bodies, were present and through the process of degeneration and necrosis a cyst was formed and later a part became neoplastic.

In Irie and Tanaka's case report[1] of primary thymic cyst, they have pointed out its extreme rarity. Thymoma itself has been cited as a relatively common tumor by Ringertz,[2] Shidler,[3] Katsura[4] and others and various classifications have shown that of the total mediastinal tumors 7.5 to 12.3 per cent were of the thymus. However, Ringertz[2] has reported that although approximately one-third of the thymus tumors seen were cyst forming, only one out of 155 cases showed a so-called thymic cyst. In Coulshed's case report,[5] the lack of suitable classification was emphasized. There are many papers dealing with malignant thymic tumors (Seybold,[6] Ringertz[2] and others) and many forms of growth seen in x-ray films and in surgery are presented. However,

FIGURE 5: Fibrous tissue and cholesterin deposits seen.

a benign thymic cyst is obviously a rare occurrence. As in Coulshed's case, the prognosis of our present case was excellent and is believed to have been timely in the diagnosis and surgery. Artificial pneumothorax together with thoracoscopic observation was the most useful diagnostic aid.

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NEW METHOD FOR ACCURATE AND RAPID DETECTION AND LOCALIZATION OF INTRACARDIAC DEFECTS AND DEFECTS OF THE GREAT VESSELS

An important addition to diagnostic methods is described which makes possible accurate and rapid detection and localization of intracardiac defects or defects of the great vessels. This procedure involves injection of an indicator, cardio-green, into selected sites in the central circulation with simultaneous recording of the concentration of this indicator in blood withdrawn from different selected sites in the right heart or pulmonary arteries and from a systemic artery. The results obtained are immediately available during the procedure.

The indicator is nontoxic in the doses used and does not cause visible discoloration of the tissues of urine. Adverse reactions as a result of the procedure have not been observed.

By means of this technic, it is possible to detect and localize intracardiac shunts which are too small for detection by determinations of the oxygen contents of blood. Furthermore, the magnitude of the left-to-right shunt, as well as the systemic and pulmonary blood flows, can be measured simultaneously from dilution curves inscribed over an interval of less than 60 seconds in duration.

These determinations can be made without the need for measurements of respiratory gas exchange or the gaseous contents of blood and are independent of variations in the oxygen content of blood or foreign gases in the blood. Active cooperation by the patient is not required, and significant loss of blood can be avoided.

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Expectoration of Foreign Body Lodged in Bronchus for 27 Years*

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A case is presented of a foreign body being expectorated after having been lodged in the bronchus for 27 years. The presence of the foreign body was not recognized and this cause for his pulmonary disease was never considered seriously during his prolonged illness. After the foreign body was recovered, he was re-examined roentgenographically and his previous chest roentgenograms were reviewed. The foreign body can be recognized on the films taken early in this illness dated October 3, 1942 (Figure 1). It can be visualized again on the more recent films taken July 13, 1954 (Figure 2). This illness is of interest because its etiology was unrecognized, although he was examined by many competent specialists in diseases of the chest and radiologists during his prolonged illness.

Case Report

The patient was first seen July 17, 1953 at the age of 44. He came to the office to be treated for an acute respiratory infection. For two days, he had had a cough productive of yellow sputum and was febrile. His temperature was 101 degrees. There was decreased expansion of the left chest and the left hemithorax was smaller than the right. The trachea was deviated to the left. There was marked diminution in breath sounds over the left chest and dullness in the same area. These changes were more marked in the lower half of the left chest. Voice sounds were equal bilaterally. The heart and mediastinum were deviated to the left. An apical diastolic gallop was

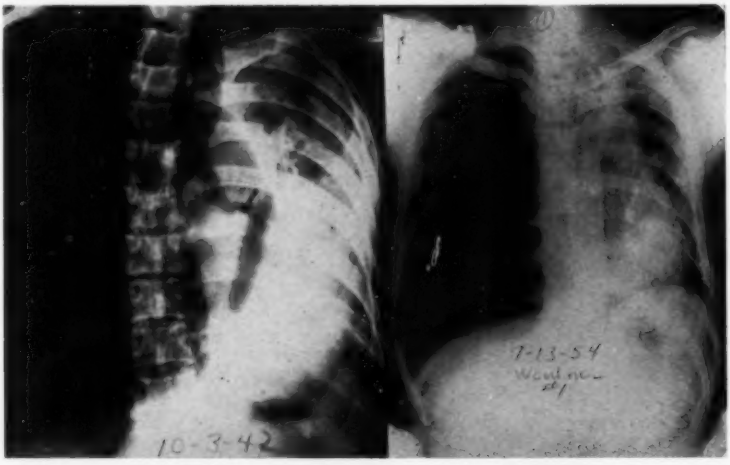

FIGURE 1 FIGURE 2

FIGURE 1: Original film shows foreign body in left main stem bronchus. FIGURE 2: Film showing foreign body just above anterior end of third rib (left).

*From the Departments of Internal Medicine and Radiology, Colorado Springs Medical Center.

present. The heart rate was 100 per minute. He refused a chest roentgenogram at that time because so many had been taken previously and he did not wish to have a comprehensive re-evaluation of his problem. At that time, he was given tetracycline, syrup of hydriodic acid, and advised to use postural drainage.

Regarding his past respiratory history, he dated his difficulty from 1931 when he developed a cold and had intermittent fever and malaise for approximately a six-month period. When examined by his physician in the fall of 1931, he was told that his difficulty was asthma and hospitalization was advised for further evaluation. Empyema of the left chest was diagnosed and treated with open drainage. The wound continued to drain for four months. At that time a thoracoplasty was advised, but refused. He was unable to work for the following 18 months because of weakness and malaise. There was some improvement, but he never regained his usual state of health. He was able to do light work. In June of 1942, he developed pneumonia and was hospitalized in a tuberculosis sanitarium with the provisional diagnosis of pulmonary tuberculosis. He was told that his sputum examinations were negative in the sanitarium, and he left the sanitarium against advice when moved into a room with a positive sputum patient. He was re-hospitalized in September of 1942. After bronchoscopy, pneumonectomy was advised for bronchiectasis of the left lung. Other doctors attending him at that time advised against this procedure and it was not performed. Again, he was able to return to light work. In 1951, because of increasing symptoms of pulmonary insufficiency and back pain, he left his home in Michigan and moved to New Mexico, later to Arizona, then California, and finally to Colorado. These moves were made in an effort to find a climate which might improve his health. During this interval of time, he had acute respiratory infections which were treated with sulfonamides, penicillin, and tetracycline.

He was seen again in our clinic a year following his initial visit with the symptoms of rapid heart action, increasing dyspnea, and nocturnal dyspnea. At that time, there was increased distention of neck veins and slight liver enlargement. The physical findings pertaining to the chest were unchanged. It was our opinion at that time that he was developing cor pulmonale with mild right sided failure secondary to his pulmonary disease. On that visit, our first chest roentgenogram was obtained which is shown in Figure 2.

The patient was digitalized, given ephedrine, and instructed in a low sodium diet.

In March of 1955, he returned to the office complaining of bloody sputum and fever and increasing difficulty in breathing. In July of 1955, he complained of severe

FIGURE 3 FIGURE 4

FIGURE 3: Foreign body which was expectorated. FIGURE 4: Chest film following expectoration of the bone.

backache in the lower dorsal area which was believed due to the spinal deformity with nerve root irritation secondary to his adhesive pleuritis. On February 7, 1956, he was showing some signs of clubbing of the fingers, but none of the toes.

In August of 1957, the patient was awakened with a severe coughing episode during which he felt an object in his mouth. He removed the object and recognized it as the cervical vertebra of a rabbit (Figure 3). On seeing this, he recalled having eaten rabbit pie in 1930 (approximately three months before the onset of his pulmonary symptoms). While eating the pie, something stuck in his throat, which he thought at the time was a rabbit bone. He took mustard water to induce vomiting. After vomiting profusely, he felt relieved and assumed the bone was in the vomitus. Not until this time did he relate the rabbit bone to his prolonged pulmonary disease. None of the many doctors who had examined him during his illness had questioned him regarding the possibility of aspirating a foreign body. Figure 4 shows a chest film following expectoration of the rabbit bone. On comparing this film with the film of the bone and the previous films, the foreign body can be recognized just above the anterior end of the left third rib.

USE OF NITROUS OXIDE WITH OXYGEN IN PAROXYSMS OF BRONCHIAL ASTHMA

A portable anesthesia apparatus was used for the administration of the gas mixture. The treatment was instituted 137 times in 108 patients suffering from bronchial asthma. Lasting effect was attained in 119 cases, a short-term improvement occurred in 12 and in six cases, the therapy was ineffective. The above mixture is particularly indicated when bronchial asthma is coupled with stenocardia. No complications were observed.

Smolinsky, K. I.: "The Use of Nitrous Oxide with Oxygen in Paroxysms of Bronchial Asthma," *Soviet Medicine*, 10:117, 1960.

ON THE FACILITATION OF ANATOMO-FUNCTIONAL SUBSTITUTION OF THE LUNG

Monaldi and Fioretti state that in cases with bronchopulmonary malformations, the diseased lung and the mediastinum may represent an obstacle to anatomo-functional substitution and compensation by the sound lung on the opposite side. They carried out experiments on puppies, subjecting them to pneumonectomy with a large opening of the posterior-inferior and anterior-superior mediastinum. Two to three months after the intervention, radiologic, bronchographic, angiopneumographic investigations and post-mortem findings showed that segmental branches of the superior and inferior lobe shifted to the opposite hemithorax in order to fill up the residual space of pneumonectomy.

Monaldi, V., and Fioretti, G. P.: "Per Facilitare la Supplenza Anatomo-funzionale del Polmone," *Arch. Tisiol. e Mal. Appl. Resp.*, 15:935, 1960.

X-RAY FILM OF THE MONTH

Edited by Benjamin Felson, M.D.

Clinical History

This patient is a 53 year-old white school teacher. He had experienced good health until June, 1958 when he began to notice "kernels" in his neck and groin. He visited the local physician who made the diagnosis of chronic lymphatic leukemia on the basis of peripheral blood examinations and bone marrow studies. Chlorambucil treatment was instituted.

He was maintained fairly well with this regimen along with periodic x-ray treatments to node bearing areas.

On April 27, 1959, he was admitted to the University Hospital for further treatment. This included TEM and multiple blood transfusions. While in the hospital, he developed several furuncles on his arms. These responded to chloromycetin therapy.

On May 23, 1959, he became nauseated. In the following 72 hours, he became lethargic and on May 28, 1959, he was stuporous. A lumbar puncture on May 24, 1959 revealed turbid fluid with normal pressure.

Chest x-ray film in April, 1959 (Fig. 1) showed bilateral hilar adenopathy. Chest x-ray film on June 19, 1959, showed bilateral adenopathy with a discrete focus of infiltration in the right upper lung field (Fig. 2).

Diagnosis: DISSEMINATED CRYPTOCOCCOSIS COMPLICATING CHRONIC LYMPHOCYTIC LEUKEMIA

He died June 3, 1960. India ink preparations done on the turbid spinal fluid on May 24, 1959 revealed cryptococcosis. Autopsy studies showed evidence of nodal enlargement in the hila and mediastinum. The nodes were packed with abnormal lymphocytes and *Cryptococcus neoformans* organisms. This same organism was obtained on culture of the meninges, lungs, and spleen.

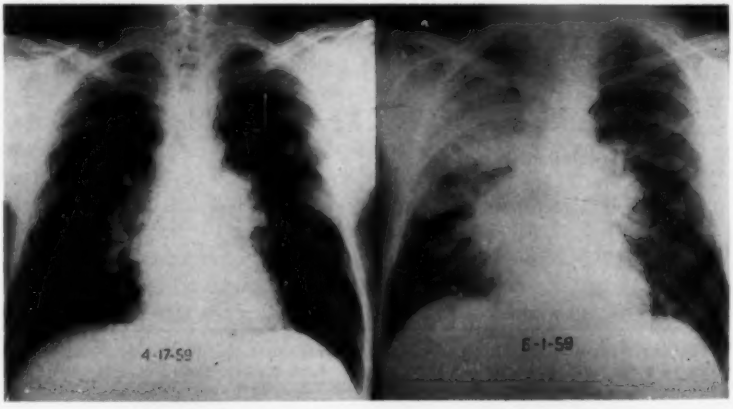

FIGURE 1 FIGURE 2

The final diagnoses were:

1. Chronic lymphocytic leukemia
2. *Staph. aureus* furunculosis
3. Cryptococcosis, disseminated

Discussion

Cryptococcosis and malignant diseases of the reticulo-endothelial system have been described together many times. A study by Zimmerman and Rappaport[1] showed that 30 per cent (24 of 74) of cases of cryptococcosis on file at the Armed Forces Institute of Pathology occurred in patients with Hodgkin's disease, reticulum cell sarcoma, leukemia, or multiple myeloma. This unusual association was attributed to the increased susceptibility of these patients to infections. The increased susceptibility may result from alterations in the hematopoietic tissues whose normal functions include antibody production.

Keye and Magee[2] found, in a study of 88 cases of fungal disease, that the incidence of primary fungal disease has not changed since 1947, but a striking increase has occurred in infections complicating lymphomas and leukemias. This included histoplasmosis, mucormycosis, candidiasis, and aspergillosis in addition to cryptococcosis. They attributed the sharp rise in the incidence of fungal infections to the treatment of lymphomas and leukemias. Some of the agents used, such as cortisone, folic acid antagonists, and 6-mercaptopurine, increase the individual's susceptibility to infection.

Klatte *et al.*,[3] in studying 121 autopsied cases of leukemia, found an incidence of 60 per cent with hilar and mediastinal lymphadenopathy. Only 15 per cent had x-ray film evidence of nodal enlargement. On histologic study, 31 per cent had leukemic infiltrations within the lung, but only seven of these 33 cases had x-ray film evidence of leukemic infiltrations in the lungs. This was in the form of a diffuse peribronchial infiltration.

In contrast to leukemic infiltrations, x-ray film evidence of pulmonary infiltrations were noted in 30 per cent of 341 cases of leukemia (only 121 autopsied cases). The clinical course, bacteriology, and response to antibiotics suggested that these were pneumonic in origin. These infiltrations were usually limited to a single lobe as opposed to the diffuse peribronchial leukemic infiltrations.

Cryptococcosis, when occuring as a secondary infection, is usually widely disseminated. This is less common in the primary disease. Unless subtle changes in the clinical course of patients suffering from malignant disease of the reticulo-endothelial system are studied carefully, the diagnosis of secondary fungal disease will be made only late in the course of the disease or at post-mortem.

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The Committee on Chest Roentgenology welcomes comments. We would also be pleased to receive x-ray films of exceptional interest with brief history. Please submit material to: Benjamin Felson, M.D., chairman, Department of Radiology, Cincinnati General Hospital, Cincinnati, Ohio.

SECTION ON CARDIOVASCULAR DISEASES

The Physiologic Advantage of Oxygen During Exercise in Patients with Coronary Artery Insufficiency*

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Previous clinical and physiologic studies have indicated that ischemic oxygen want is the fundamental physiologic defect in coronary artery insufficiency, and that anginal pain is caused by myocardial hypoxia.[1,2] The value of oxygen therapy in coronary thrombosis, cardiac insufficiency and severe angina pectoris is well-recognized;[3-6] however, the administration of oxygen has heretofore been limited to patients at rest.

A theoretical justification for the use of oxygen during exercise in coronary insufficiency was provided by Master, who showed that many patients with coronary disease develop electrocardiographic abnormalities following exercise, comparable to those elicited by the inhalation of low-oxygen mixtures in similar cases;[7,8] he attributed this response to the production of myocardial anoxemia by exercise.[9]

The recent development of portable apparatus suitable to the patient and the physician, which makes possible the ambulatory use of oxygen has prompted us to study the relative effects of oxygen inhalation on the electrocardiograms of patients with coronary insufficiency both at rest and during the performance of the standard Master two-step test.

Material and Methods

A group of 22 patients with clinical coronary insufficiency was studied. Nineteen were considered to have arteriosclerotic heart disease; of these, seven also had a history of old or recent coronary occlusion, and seven had angina pectoris. Two others had cor pulmonale, and one had a severe megaloblastic anemia with angina pectoris. Eleven were receiving digitalis.

Electrocardiographic tracings were taken in 12 leads on all patients while resting in the supine position breathing room air. Oxygen was then administered at 12 to 15 liters per minute by means of a loosely-fitting plastic face mask and the tracings were repeated in leads L_2, V_2, and V_4, in 2, 5, 10, and 15 minutes.

Ten patients were considered unsuitable for exercise. The remaining 12, after a rest period of 15 minutes or longer, were subjected to a standard Master two-step exercise while breathing room air. After exercise, they were returned to the supine position and tracings in L_2, V_2 and V_4

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were taken immediately, 2, 5, 10, and 15 minutes later. One hour to two days later the exercise test was repeated while the patients inhaled oxygen at 12 to 15 liters per minute through the plastic face mask which was connected by a long rubber tube to a standard oxygen tank. When the two exercise tests were not performed in the same day, the second test was preceded by a resting control electrocardiogram. Post-exercise tracings were taken in the identical manner as following exercise with air.

The height and direction of the ST segment (or J-Point) and T waves were measured in all tracings to the nearest tenth of a millimeter and corrected for standardization. Tracings taken at rest on air were compared with those taken five minutes after the start of oxygen inhalation, and changes of 0.5 mm. or more in either direction of the ST segment and T wave were tabulated. The changes between baseline tracings at rest on air, and those occurring two minutes following exercise breathing air were compared with corresponding changes in the same patient from a similar baseline in the tracings taken two minutes after exercise breathing oxygen. Post-exercise ST segment depressions were interpreted as significant of myocardial ischemia when they reached or exceeded 0.5 mm., when the configuration of the depressed segment was of the "ischemic" type[10] and when the time duration of the depressed RS-T segment exceeded 50 per cent of the QT interval in the same ventricular response.[11,12]

Results

A. *Effect of Oxygen Inhalation on the Resting Electrocardiogram:*

Electrocardiographic changes following the inhalation of oxygen at rest occurred in 14 of 22 patients (Figure 1). Three showed only ST segment changes, two both ST and T changes, and nine T wave alterations. Elevation of the T wave was the most frequent change observed and occurred in seven patients, in four of which the rise was 0.8 mm. or greater (Figure 2). Four showed lowering of the T waves.

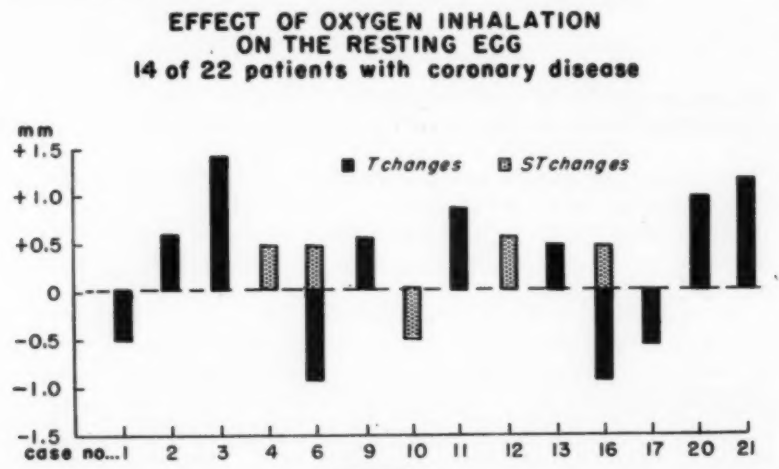

FIGURE 1

B. *Effect of Oxygen Inhalation on the Master Two-Step Test:*

Ten of the 12 patients tested showed significant ischemic ST segment depressions of 0.5 mm. or greater, following the performance of the Master two-step test while breathing air. In eight of these patients, there was less ischemic ST segment depression when the same exercise was performed during the inhalation of oxygen. In six instances, the Master test became negative after exercise with oxygen, since the corresponding ischemic ST segment depressions were reduced to less than 0.5 mm. from the resting controls; this occurred in spite of the fact that four of these patients were on digitalis (Figure 3). In the other two, the degree of ischemic ST segment depression after exercise with oxygen was markedly diminished; however, the Master tests after exercise on oxygen were still positive (Figure 4). In these two, the appearance of the tracings after exercise on oxygen is more similar to that of the resting controls; both cases showed ischemic ST depressions after exercise with air which assumed the "junctional" pattern in contour and duration after exercise with oxygen. One, who had a slightly greater ST depression in L_2 after exercise on oxygen than after exercise with air, also showed in lead V_2 a junctional depression in the resting control which became ischemic after exercise with air and returned to junctional after exercise with oxygen. In one, the same changes occurred after exercise with air as after exercise with oxygen.

Two of the cases studied did not show positive Master tests after exercise on air or on oxygen: one showed a greater degree of junctional ST depression after exercise on air and the other developed greater T wave changes after exercise on air.

The only patient in whom similar changes were noted after the two methods of exercise had anginal pain and an associated megaloblastic anemia of Hb. 7.1 gm. and RBC of 2.38 million/cu. mm. It is possible that her deficient oxygen transport system accounted for the persistently abnormal post-exercise electrocardiograms.

All the patients appeared to tolerate the exercise better while inhaling oxygen. Two patients who developed angina at the end of the procedure when breathing air had no precordial pain upon exercising breathing oxygen.

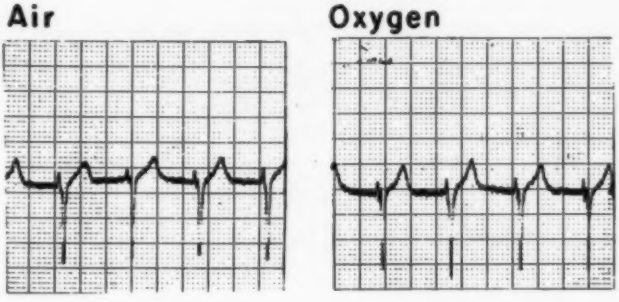

FIGURE 2: Lead V_4 showing elevation of T wave after inhalation of oxygen at rest.

Discussion

The electrocardiographic changes described in this study may be interpreted as resulting from the inhalation of oxygen itself, and not from other factors. It is known that hyperventilation can produce ST and T changes in the electrocardiogram, similar to those of coronary insufficiency, and that the inhalation of CO_2 can prevent such changes.[13,14] In the present series, rebreathing of CO_2 was prevented by the high flow of oxygen into a loosely-fitting face mask which fostered elimination of exhaled CO_2 into the surrounding air; in addition, an inspiratory valve ahead of the collecting bag did not permit rebreathing.

The inhalation of oxygen at rest produced a variety of electrocardiographic changes, generally of slight degree. The most frequent and quantitatively greater change was elevation of the T waves. Barach and Steiner[15] described T wave elevations in 20 of 26 patients with heart disease who received 100 per cent oxygen at rest, and interpreted this response as due to a shorter recovery period of heart muscle during the use of oxygen.

In contrast with these relatively-minor changes at rest, the use of oxygen during exercise inhibited some or all of the electrocardiographic abnormalities which occurred in 11 of 12 cases when the exercise was performed on air. In these patients, oxygen inhalation during the test seemed to protect the myocardium from the hypoxic effects of exercise. Riseman and Brown[16] have found that patients with angina pectoris show improvement in exercise performance during oxygen inhalation. Gorlin *et al.*[17] found in their studies on the response to standard exercise in cases of angina that patients who failed to develop pain or ST segment changes after exercise showed an increased coronary blood flow and decreased coronary vascular resistance, with a normal coronary venous saturation, while those who had pain and ST depression showed a fixed coronary blood flow and very slight fall of coronary vascular resistance with an associated marked fall in the saturation of blood from the coronary sinus. On the basis of this evidence, the inhalation of oxygen during periods of physical activity may be recommended to patients with coronary insufficiency, particularly to those showing anginal pain or ischemic ST depressions after exercise.

The administration of oxygen to persons while they are undergoing physical exertion has been made feasible by the advent of lightweight portable oxygen apparatus that can be carried easily by the patient. High pressure cylinders containing 75 to 150 liters of oxygen are equipped with miniature two-stage regulators for delivery of a constant flow of oxygen, the total weight being three to five pounds. They may be connected to plastic face masks, nasal cannulas, or mouthpieces with a venturi, and can be refilled by the patient from a standard-sized oxygen tank by means of a special device.[18] For short periods of oxygen administration, or when maximum portability is desired, a cigar-shaped, pocket-sized four ounce metal canister, into which small disposable oxygen cartridges are inserted, is available. The oxygen is released on inspiration by a manually operated valve and is inhaled through a venturi mouthpiece which is usually set at concentrations of 32 to 40 per cent. The average duration of

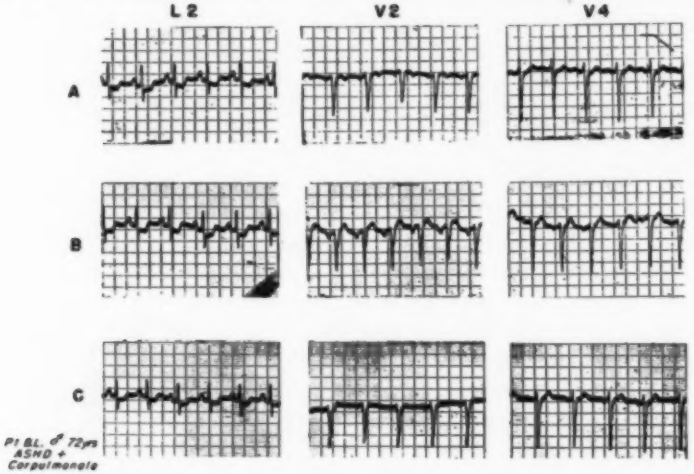

FIGURE 3: A: ECG at rest. B: ECG two minutes after exercise breathing air, showing ischemic ST depression in lead 2. C: ECG two minutes after exercise breathing oxygen, showing return of ST depression to resting control level. T waves were elevated after exercise on air.

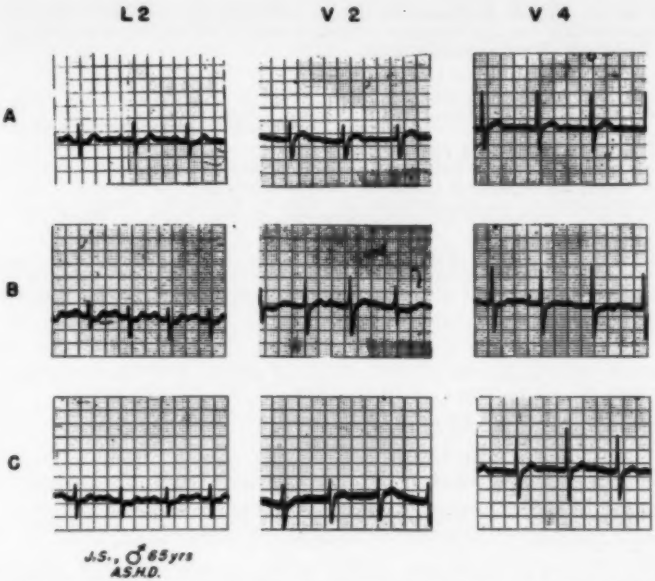

FIGURE 4: A: ECG at rest. B: ECG two minutes after exercise breathing air, showing ischemic ST depression in L_2 of 0.9 mm. below resting control. C: ECG two minutes after exercise breathing air, showing reduction of ST depression in L_2 to 0.5 mm. below control. T wave in V_4 is flattened after exercise on air and resembles resting control after exercise on oxygen.

oxygen inhalation of from one to one and a half minutes per cartridge is prolonged to 10 to 15 minutes if nine small cartridges are carried as an extra supply. The cartridge changes may be accomplished in eight seconds by the trained subject.[19]

The clinical use of ambulatory oxygen therapy in patients with coronary artery insufficiency may be extended beyond its application during exercise periods producing myocardial hypoxia. Patients with angina pectoris may be able to benefit from a program of graduated exercise with oxygen, similar to the one now being used with advantage in the rehabilitation of cases of chronic pulmonary disease.[20] Exercise with oxygen may also permit a more rapid convalescence of the patient with coronary thrombosis after a suitable period of rest. Lastly, the availability of oxygen in the home of patients with coronary disease, or in the doctor's bag, will lead to its immediate use in acute coronary thrombosis, at the crucial time when delay may mean the difference between life and death.

SUMMARY

1. The inhalation of oxygen at rest produced electrocardiographic changes in 14 of 22 patients with clinical coronary artery insufficiency. Elevation of the T wave occurred in seven.

2. The inhalation of oxygen during a standard Master two-step test inhibited some or all of the electrocardiographic abnormalities which occurred when the same exercise was performed breathing air, in 11 of 12 cases. In nine, there was decrease of ST segment depression when the exercise was performed with the aid of oxygen.

3. The use of oxygen during periods of exercise producing myocardial hypoxia in patients with coronary insufficiency appears to be a new approach that deserves additional physiologic study and clinical use.

RESUMEN

1. La inhalación de oxígeno en reposo produjo cambios electrocardiográficos en 14 de 22 enfermos con insuficiencia arterial coronaria clínica. La elevación de la onda T se presentó en 7.

2. La inhalación de oxígeno durante la prueba estandard de Master, de los dos escalones, inhibió algunas o todas las anormalidades electrocardiográficas que ocurrieron cuando el mismo ejercicio fue practicado respirando aire, en once de doce casos. En nueve de ellos hubo disminución de la depresión del segmento ST cuando el ejercicio se llevó a cabo con ayuda de oxígeno.

3. El uso de oxígeno durante períodes de ejercicio que producen hipoxia del miocardio en enfermos con insuficiencia-coronaria parece ser un nuevo método que merece estudio fisológico adicional y uso clínico.

RESUMÉ

1. L'inhalation d'oxygène au repos a créé des modifications électrocardiographiques chez 14 des 22 malades atteints d'insuffisance clinique de l'artère coronaire. L'élévation de l'onde T survint chez 7 malades.

2. L'inhalation d'oxygène pendant le test standard des "deux marches" inhiba certaines ou toutes les anomalies électrocardiographiques qui survenaient lorsque le même exercise était pratiqué en respirant de l'air pour 11 des 12 cas. Dans 9 cas, il y eut une diminution de la dépression du segment ST lorsque l'exercise fut pratiqué avec l'aide de l'oxygène.

3. L'utilisation d'oxygène pendant des périodes d'exercise produisant une hypoxie myocardique chez les malades atteints d'insuffisance coronarienne semble être une nouvelle tentative qui mérite une étude physiologique supplémentaire et un application clinique.

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Transmural Ventricular Pressures and Pulsus Paradoxus in Experimental Cardiac Tamponade*,**

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Cincinnati, Ohio

The studies to be reported in this paper have been made with the dual purposes of shedding further light on the occurrence of ventricular suction and of elucidating further the mechanism of pulsus paradoxus. Bloom[1,2] awakened the present interest in the topic of ventricular suction when he demonstrated that the excised rat heart placed, still beating, into isotonic saline fills and empties repeatedly, causing the organ to be rapidly and forcefully propelled around the container. Under normal circumstances the *vis a tergo* provided by the venous return is thought to be the principal force responsible for cardiac filling. Under these circumstances, the ventricular transmural diastolic pressure is higher than atmospheric pressure. Under the abnormal circumstance of embarrassed venous return, however, ventricular diastolic suction may develop as an auxiliary filling mechanism. Several experiments designed to measure the ventricular diastolic pressure during conditions of reduced venous return have been reported. In these experiments the transmural diastolic pressure in the ventricle has been found to be subatmospheric. Thus, Brecher[4] decreased the return of blood to the left ventricle in dogs by means of experimental blockage of the mitral valve and was able to measure negative transmural pressure in the left ventricle during diastole. Similarly Bloom and Ferris[3] and Fowler, Couves and Bewick,[5] working with the right side of the dog heart, obstructed inflow to the right ventricle and demonstrated right ventricular negative diastolic transmural pressure. Fowler *et al.*[5] measured the left ventricular pressure in dogs during rapid exsanguination and found that it was negative during diastole.

Pericardial effusion with tamponade is yet another condition which may be expected to interfere with diastolic filling of the heart and thus be associated with negative transmural diastolic pressures. Since Kussmaul's original description in 1873,[7] cardiac compression has been known to cause "a regular rhythmic variation in the pulse while the heart beat remains constant. With each inspiration, at regularly repeated intervals, the pulse becomes smaller—to return again with expiration." The present paper describes some of the alterations produced in the circulation of the dog by experimental cardiac tamponade. The majority of studies reported here were made in animals with open chests. Further studies with the closed chest preparation are continuing and a preliminary report on them is included in this paper. Several investigators have

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Work accomplished during Dr. Shabetai's tenure of a Research Fellowship of the American Heart Association.
**Presented at the 26th Annual Meeting, American College of Chest Physicians, Miami Beach, Florida, June 8-12, 1960.

studied the effects of experimental cardiac tamponade on the circulation. Many of these studies were published before sensitive apparatus for the recording of detailed pressure pulses had been developed. For example, Starling[8] was one of the first to inject mineral oil into the pericardial sac. He demonstrated that with cardiac compression, the systemic venous pressure rose and the systemic arterial pressure fell. Katz and Gauchat[9] published their classical experiments on the paradoxical pulse in 1924. Metcalfe *et al.*[10] measured the pressures in the right atrium, pulmonary veins, great vessels and pericardial sac during experimental tamponade. They found that with increasing intrapericardial pressure, the right atrial and pulmonary venous pressures rose equally. They did not measure ventricular pressures and thus were not prepared to make observations upon ventricular diastolic suction. They did not report negative pressure in the atria but stated that when the intrapericardial pressures were elevated to about 20 mm. Hg., all intravascular pressures tended to approach the same value of about 20 mm. Hg. Although they measured the pulmonary arterial and systemic arterial pressures, they made no

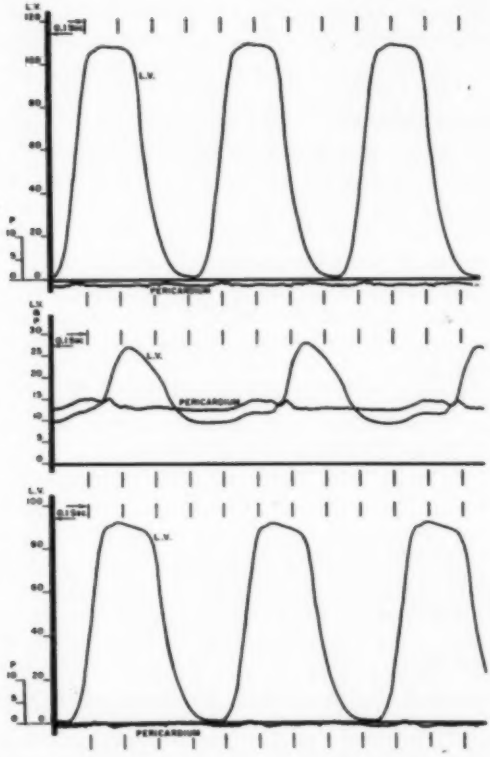

FIGURE 1: Left ventricular and intrapericardial pressures from an open chest dog *before* (above), during (middle), and after (below) the production of cardiac tamponade. Pressures mm. Hg; paper speed 200 mm./sec. Left ventricular pressure recorded at twice control sensitivity during cardiac tamponade. Reproduced from Fowler *et al.*,[5] Figure 2, *Circulation Research*, Vol. VII, no. 5, 1959, by kind permission of the editor of *Circulation Research*.

comment upon pulsus paradoxus. Evans *et al.*[11] observed a narrow pulse pressure in the right ventricle due to an elevation of the diastolic pressure without increase in the systolic pressure during tamponade. In their animals the ventricular diastolic pressure remained equal to, or slightly greater than, the intrapericardial pressures. Their paper was not concerned with the paradoxical pulse. Our experience with open chest dogs led us to the conclusion that experimental cardiac tamponade in closed chest dogs would be an excellent preparation with which to study the phenomenon of the paradoxical pulse and also that of ventricular suction.

Method

Open Chest Animals. The method has been described by Fowler *et al.*[8] Briefly, a bilateral thoracotomy was performed and two cannulae, one for recording pressure and the other for the injection and aspiration of saline, were sutured in water-tight fashion into the pericardial sac. Side-hole cannulae were inserted into the cardiac chambers where pressure was to be measured (usually both ventricles and the right atrium) and purse strings in the pericardium were tightened around them. Pressures were measured by Statham P23Db gauges and recorded at paper speeds

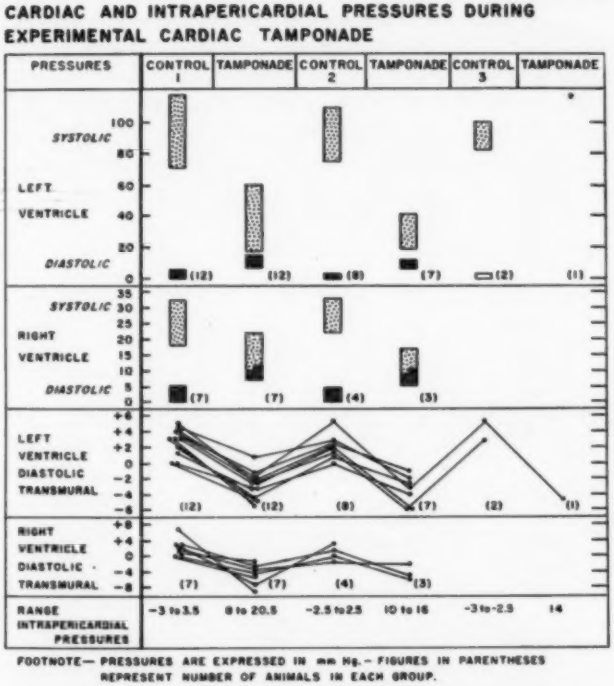

FIGURE 2: Range of change in left and right ventricular systolic and diastolic pressures and individual changes in ventricular diastolic transmural pressupres before, during and after experimental tamponade. Pressures mm. Hg.; figures in parentheses —number of animals in each group. Reproduced from Fowler *et al.*,[8] Figure 1, *Circulation Research*, Vol. VII, No. 5, 1959, by kind permission of the editor of *Circulation Research*.

of 200 mm./sec. and at sensitivities of 1 cm. deflection for 5 mm. pressure on an Electronics for Medicine recorder. Reversible cardiac tamponade was produced by injecting saline into the pericardial sac. Comparisons were then made between the pericardial and intracardiac pressures before, during and after the induction of tamponade.

Results

Satisfactory data were obtained from 13 of 20 dogs. As the intrapericardial pressure rose during the injection, the systolic pressure in the ventricles fell and the diastolic pressure rose, but as the injection continued, the rise in ventricular diastolic pressure failed to keep up with the increase in the intrapericardial pressure and there resulted, therefore, negative transmural pressures in the ventricles. In other words, potential suction was demonstrated. Figure 1 illustrates a typical run from the left ventricle. The transmural pressure is seen to be slightly positive in the control and recovery tracings. During tamponade, a negative transmural pressure of 2.5 mm. Hg. is seen. Except in one instance, negative transmural pressures were found in both ventricles when the pressures from these chambers were measured simultaneously, or from

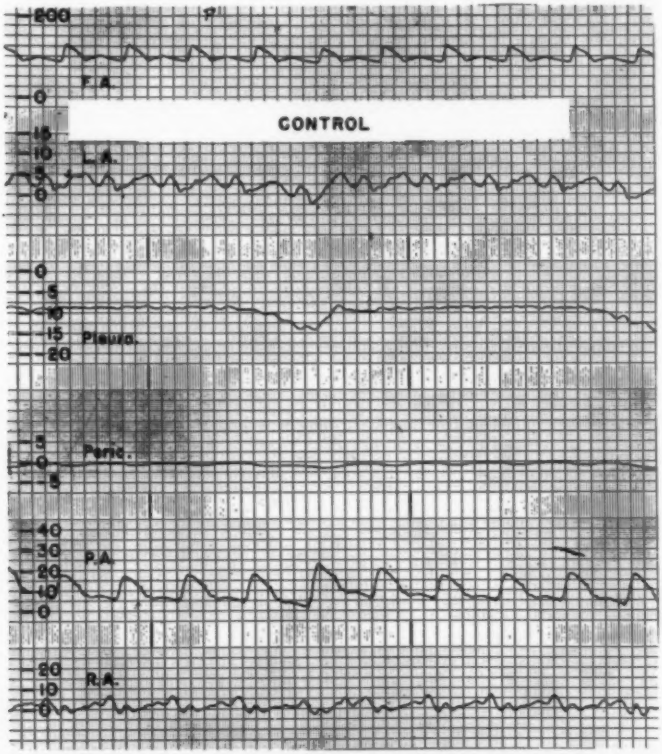

FIGURE 3A: Pressure record of closed chest dog from the femoral artery, left atrium, pleural space, pericardial space, pulmonary artery and right atrium *before* tamponade. Pressures mm.Hg.; paper speed: 200 mm./sec.

the left or right ventricle, when only one ventricular pressure was measured. Figure 2 summarizes the amount of negative transmural ventricular pressure obtained and the number of times that it was produced.

In general, only small increases in the intrapericardial pressure were required to lower the systolic pressure of both ventricles. The intrapericardial pressure exceeded the left ventricular diastolic pressure earlier and at lower levels than was the case with the right ventricle.

Analysis of the records indicated that, with severe tamponade, high intrapericardial pressures may exceed not only the diastolic pressure in the right ventricle but its systolic pressure as well. Furthemore, it was frequently noted that systole in the right venticle was shorter than it was in the left. The phenomenon of the "early diastolic dip" described by Hansen and co-workers[11] in constrictive pericarditis in man was not observed in the vast majority of tracings.

Closed Chest Preparation Method. A standard left thoracotomy was performed on mongrel dogs anesthetized with sodium pentobarbital and

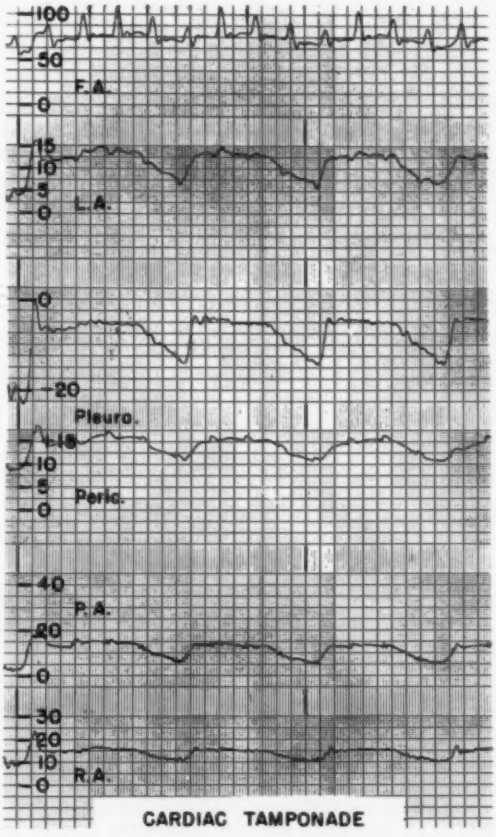

FIGURE 3B: Pressure record of closed chest dog from the femoral artery, left atrium, pleural space, pericardial space, pulmonary artery and right artium *during* tamponade. Pressures mm.Hg.; paper speed: 100 mm./sec.

positive pressure respiration. Two Sanborn connector tubings were sewn into the pericardial space. The left atrium was cannulated in retrograde fashion through a segmental pulmonary vein with a No. 7 cardiac catheter. The pulmonary artery was cannulated via a segmental branch. The ascending aorta was cannulated from the femoral artery by a No. 8 cardiac catheter. The two pericardial cannulae, the catheters in the pulmonary vessels, and a catheter whose tip lay in the pleural space were brought out through the incision and the chest was carefully closed. After all leaks had been eliminated, the respirator was disconnected and the dog was permitted to resume spontaneous respirations. In some instances the ventricles were punctured percutaneously with long No. 18

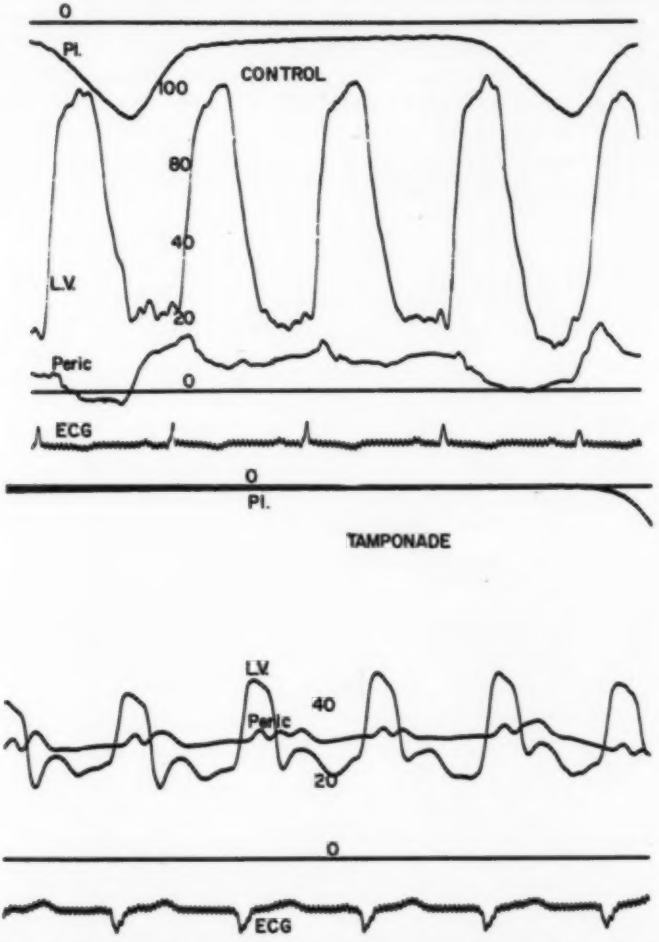

FIGURE 4: Left ventricular negative transmural diastolic pressure. Control (above); tamponade (below). Paper speed, 100 mm./sec.; pressures, mm.Hg. From above, down; Zero line for pleural pressure; pleural pressure; left ventricular pressure; intrapericardial pressure; common zero line for left ventricular and intrapericardial pressures; and electrocardiogram. The catheter and gauge for the pericardial sac were 2.5 cm. of water higher than those for the left ventricle.

needles, and in others the ventricles were catheterized from the jugular vein or the femoral artery. The right atrium was catheterized from the femoral vein.

In a small pilot group, simultaneous pressures were measured on an eight channel Sanborn recorder from the pleural cavity, the pericardial space, both atria, both ventricles and both great vessels, before, during and after the induction of tamponade. This survey revealed that it is possible to record subatmospheric transmural pressures from all cardiac chambers during cardiac tamponade. In the present studies, which are still in progress, the chambers are being studied individually, or in pairs, and the pressures are being recorded on an Electronics for Medicine recorder. The catheter tips in the left atrium and pulmonary artery were at identical vertical heights from the table top. The catheter tips in the remaining cardiac chambers and vessels were arranged so that, where possible, they were at the same height as the previous two catheters. The heights of all were measured before closing the chest and were checked at autopsy. The catheters in the pericardial sac were placed for technical reasons 2 to 4 cm. above the intracardiac catheters. All gauges were set to the same height as their corresponding catheters. This arrangement precluded the possibility of false elevation of the intrapericardial pressure (and thus, reduction of the transmural pressure) from differences in hydrostatic zero. Records were made at paper speeds of 200 mm./sec. Pressures were recorded on Statham P23Db gauges which were set at equal sensitivities. To study the transmural pressure, the intrapericardial pressure and the intracardiac pressure were recorded from a common zero line and gain was adjusted so that five of the seven available inches of paper width were occupied by the largest deflections.

Results

In the control and recovery tracings the ventricular diastolic pressures and the atrial pressures were higher than the pericardial pressure throughout the respiratory cycle. In the eight dogs studied to this time, the arterial systolic and pulse pressures decreased 5 to 10 mm. Hg. with inspiration. The pulmonary arterial pressure was highest shortly after the aortic pressure was lowest with respect to the respiratory cycle. In other words, the respiratory variation in the aortic and pulmonary arterial tracings was almost 180 degrees out of phase. With cardiac tamponade, pressure declined still more during inspiration, but, as in the control, during inspiration the pulmonary arterial pressure was maximal while the aortic pressure was minimal.

In addition to the enhancement of the respiratory variation, increasing intrapericardial pressure consistently induced other hemodynamic alterations. The systolic pressures in the greater and lesser circulations were decreased while the diastolic pressures rose. As with the open chest preparation, the increase in diastolic pressures failed to keep up with the increase in the intrapericardial pressure and there resulted first in the left ventricle, and later in the right ventricle, negative transmural pressures. The transmural pressures in the atria likewise became negative. During this period, the heart rate increased. If the intrapericardial pressure was increased above 15 mm. Hg. to between 20 and 25 mm. Hg.,

marked bradycardia, often with a ventricular pacemaker ensued, and the intrapericardial pressure exceeded the systolic pressures in the ventricles. Prompt removal of the intrapericardial liquid resulted in a restoration of the circulation followed by a period of overshoot in which there was tachycardia and marked hypertension. After a variable period, the heart rate and blood pressure returned to control levels.

Figure 3a is from a closed chest dog before the production of experimental cardiac tamponade. During inspiration (negative deflection of the pleural tracing) the blood pressure is 120/85. In expiration the pressure is 130/90. The corresponding pressures recorded from the pulmonary artery are 23/2 and 17/6. The respiratory variation of these two pulses is thus seen to be opposite in direction. It must be noted that the net femoral artery pressure is the pressure recorded on the gauge. To obtain the net pulmonary arterial pressure, the sign of the intrapleural pressure must be changed and the amount added to the recorded artery pressure. With this correction, the pulmonary artery pressure reads 35/14 during inspiration and 26/15 in expiration.

Figure 3b records the findings during tamponade. The pericardial pressure has been elevated from minus 1 mm. Hg. to 15/6. The paradoxical pulse is now extreme. When the intrapericardial pressure was half way between the control and the tamponade value (not shown) the pulmonary artery pressure pulse showed a marked respiratory variation, opposite in direction from that in the femoral arterial tracing. With the more severe tamponade present, it can be noted that the pulmonary artery pressure pulse has practically disappeared and that the variation in the pulmonary arterial pressure is almost entirely respiratory. Subatmospheric pressures are beginning to be recorded from both atria during inspiration. When the tamponade was increased in this animal, the intrapericardial pressure finally exceeded that in the atria throughout the respiratory cycle. Negative transmural pressures were measured on several occasions from one or more cardiac chambers in 7 or 8 dogs studied to this time.

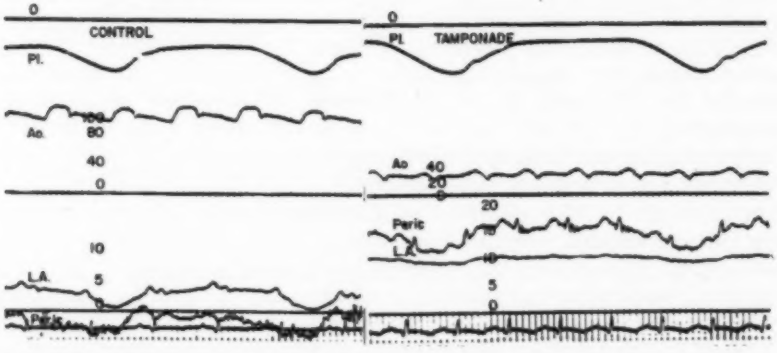

FIGURE 5: Negative transmural pressures in the left atrium. Paper speed, 75 mm./sec.; pressures, mm. Hg. Control (above); tamponade (below). From above, down; Pleural zero line; pleural pressure; aortic pressure; left atrial pressure and intrapericardial pressure. In the tamponade, the left atrial and intrapericardial pressures are reversed. Time lines 0.04 sec. The catheter and gauge for the pericardial sac were 2.5 cm. of water higher than those for the left atrium.

Figure 4 demonstrates the appearance of negative transmural pressure in the left atrium of a closed chest dog. The record from which this illustration was made was obtained after three previous runs. Figure 5 illustrates negative transmural diastolic pressure in the left ventricle of a closed chest dog.

Discussion

It is exceedingly difficult to record intraventricular pressure tracings that are free from overdamping on the one hand or fling artefacts on the other. Scheu and Hamilton[13] have recently suggested that before a left ventricular tracing may be considered satisfactory, the systolic pressure must agree within 8 mm. Hg. with that in the aorta; that there should be a small early diastolic dip toward, but not below, zero; and that the diastolic portion of the curve should move in a parallel way with the intrapleural curve. Every attempt was made to meet these criteria. Where they were not met, the changes were so consistent and reproducible and of such magnitude that it was believed that they could not be accounted for by artefact. In this connection, it was particularly desirable to confirm the presence of diastolic suction in the atria as well as in the ventricles. Satisfactory intra-atrial curves are much more readily obtained and the hazard of fling artefact is correspondingly very much reduced.

The results obtained are compatible with the hypothesis that decreased venous return is responsible for decreased ventricular diastolic volume and, thus, for negative transmural diastolic pressure.[14] During cardiac tamponade, diastolic filling of the ventricle is inhibited and venous return is hampered. There may thus develop a critical ventricular diastolic volume with respect to cardiac filling at which subatmospheric transmural diastolic pressure may be measured. Critical ventricular diastolic volume may likewise explain the subatmospheric transmural diastolic pressures recorded during experimental blockage of the venous return and during rapid hemorrhage. Subatmospheric transmural ventricular diastolic pressures have not been recorded in the normal circulation although this does not exclude the possibility of suction aiding filling even under normal circumstances. For a critical review of this subject, the reader is referred to Brecher.[15]

During the periods where the intrapericardial pressure was made to exceed the systolic pressure in the ventricles, it is doubtful that any flow was occurring. So far, we have not attempted to measure flow or ventricular volume during experimental cardiac tamponade.

Several of our findings tend to support the observations of Burwell[16] that during tamponade the contribution of the right ventricle to the pressure head in the pulmonary circulation is not great. In the open chest animals, as well as in the closed chest ones, the systolic pressure in the right ventricle did not always exceed that in the pericardial sac. This abolition of the right ventricle as an effective pump did not necessarily signal a marked fall in the left ventricular pressure. In the closed chest dogs, the right ventricular pressure pulse could be reduced to a non-pulsatile curve which faithfully followed the intrapleural pressure tracing. The level of this smooth curve was below that of the intrapericardial trace throughout the cardiac and respiratory cycles (Figure 3b).

The severe shortening of the duration of right ventricular systole, as compared to that simultaneously recorded from the left ventricle, suggests that this thin-walled structure is more completely compressed and that systolic duration is decreased in proportion to the decrease in the volume of systolic discharge and in pulmonary vascular resistance.

The observations on the nature of pulsus paradoxus are interesting. These observations are best made with moderate degrees of tamponade since the more severe degrees result in abolition of the right ventricular pressure pulse (Figure 3). With more modest elevations of intrapericardial pressure, the normal inspiratory decline of aortic pressure is greatly exaggerated. Hypotheses which are based upon the assumption that cardiac tamponade abolishes the normal increment of right heart pressure with inspiration are not supported by this study.

Katz and Gauchat[9] found that in experimental cardiac tamponade inspiration lowers the right atrial pressures less than it lowers the pressure in the extrapericardial portion of the superior vena cava. They concluded that in tamponade, inspiration creates an unfavorable change in the gradient between superior vena cava and right atrium and thus impairs right heart output. Furthermore, they "extrapolated" their results to apply to the left atrium and pulmonary veins as well. We have made measurements which suggest that both these assumptions may be erroneous. First, we have confirmed the work of subsequent workers showing that during tamponade, right ventricular and pulmonary arterial pressure *increase* during inspiration and decrease with expiration,[17,18] and secondly, respiration alters the pressure pulses of the pulmonary artery and aorta in approximately opposite directions.[17,18]

Dornhorst[17] has suggested that paradoxical pulse in cardiac tamponade is due to the interference with left ventricular filling caused by right ventricular enlargement during inspiration. He recognized that in cardiac tamponade inspiration produces an increase in the pulmonary artery pulse rather than the decrease assumed by Katz.[9]

He suggested that when left ventricular filling is embarrassed by a virtually undistensible envelope, the increase in right ventricular size that occurs during inspiration can be achieved only at the expense of the left ventricle, whose output will tend to decline at the same time as the right ventricular output increases. The fact that the pulses from the aorta and the pulmonary artery are almost, rather than precisely, 180° out of phase suggests that the explanation may not be quite as simple as that proposed by Dornhorst.

At the present time we do not have sufficient information to postulate a totally satisfactory explanation of the phenomenon of paradoxical pulse in cardiac tamponade. During normal respiration without tamponade, right ventricular filling is increased during inspiration[19] because the negative pressure that is produced in the intrapleural portion of the systemic great veins and in the right atrium creates a gradient favorable to filling from the extrapleural portion of the systemic great veins in which the pressure is positive. During cardiac tamponade, inspiration is still capable of producing an increase in the right ventricular systolic and pulse pressures. It would be erroneous to assume that because pressure is increased, flow is, ipso facto, increased as well. Eventually the relationship between pulse pressure and stroke output will have to be determined by means of a phasic flowmeter.

In the interim, there is an abundance of circumstantial evidence which suggests that increased pulse pressure is, in fact, a reflection of increased stroke volume. Shuler *et al.*[20] showed that inspiration is accompanied by an increase in right ventricular volume and suggested that right ventricular output was, therefore, increased during inspiration. Lauson *et al.*[18] observed increased right ventricular systolic and pulse pressures during inspiration and stated that inspiration increases right ventricular flow since it had been shown to increase both the pressure and the diastolic volume of the right ventricle. Brecher[19,21] has demonstrated that inspiration causes first an increase in right heart inflow and two or three beats later, an increase in right heart stroke output. The assumption that increased ventricular or arterial pulse pressure indicates a corresponding increase of ventricular stroke volume is thus supported by indirect evidence. However, until flows are measured, final conclusions may not be drawn.

The pulmonary veins are intrapleural throughout their length; therefore, inspiration cannot produce a gradient favorable to filling the left atrium in the same way that it does in the right atrium. In the normal circulation there is a slight decrease in the aortic pressure during inspiration. This has been attributed to the increased capacity of the thorax that occurs with inspiration. This hypothesis also makes the assumption that pressure changes are necessarily accompanied by flow changes and will, therefore, remain unproved until the effects of respiration upon aortic flow have been measured directly.

Paradoxical pulse may be nothing more than an exaggeration of the normal phenomenon. In addition, there may be other factors such as that suggested by Dornhorst.[17] When studies have been completed demonstrating the effects of respiration upon directly measured flows in the pulmonary artery and aorta, it will be known if the decrease in the systemic pulse during inspiration reflects decreased flow, decreased peripheral vascular resistance or simply the transmission of negative pressure from the thorax to the left heart.

SUMMARY

Transmural pressures were measured from both cardiac ventricles before, during and after experimental cardiac tamponade in open chest dogs. During the control and recovery periods, the transmural pressures were positive in both ventricles. During tamponade, the transmural diastolic pressures became negative in both ventricles.

In a series of closed chest dogs, subatmospheric transmural pressures were measured during cardiac tamponade from both atria and both ventricles. With severe tamponade, the intrapericardial pressure exceeded the right ventricular systolic pressure, and with very severe tamponade, even the left ventricular transmural systolic pressure was negative.

In the control and recovery tracings, inspiration was accompanied by an increase in the pulmonary arterial pulse pressure and a simultaneous decrease in the aortic pressure pulse. This phenomenon was exaggerated during cardiac tamponade. The implications of this finding regarding the genesis of pulsus paradoxus were discussed.

ADDENDUM: Since submitting this paper for publication, the authors' attention has been drawn to an abstract by Drs. Manning and Brecher published in *Federated Proceedings*. It deals with negative transmural ventricular pressures in open chest preparations. (Manning, J. W., and Brecher, G. A.: "Negative Transmural Ventricular Pressures in Experimental Pericardial Effusion," *Federated Proceedings*, 18:97, 1959).

RESUMEN

Se midieron las presiones transparietales tanto de los ventrículos antes, como durante y después de repleción pericárdia experimental en el tórax abierto de perros. Durante el contro ly el período de recuperación, la presión transparietal fué positiva en ambos ventrículos. Durante la repeleción las presiones diastólicas transparietales se hicieron negativas en ambos ventrículos.

En una serie de tórax cerrado en perros, las presiones subatmosféricas transmurales se midieron durante la repleción pericárdia tanto en aurícula como en ventrículo. Con la repleción intensa la presión intrapericárdia excedió la presión ventricular sistólica derecha, y con repleción muy severa, aún la presión transparietal sistólica ventricular izquierda fué negativa.

En el control y durante los trazados de la recuperación la inspiración se acompañó de una aumento de la presión del pulso en la arteria pulmonar. Este fenómeno fué exagerado durante la repleción pericárdia. Se diserta sobre lo que puede implicar este hallazgo respecto del pulso paradójico.

(N. del T.) El término taponamiento cardiaco ha venido usándose en Español como traducción de tamponade tratándose de *repleción pericárdia* palabra que es mas correcta.

RESUMÉ

Les pressions transmurales furent mesurées à partir des deux ventricules cardiaques avant, pendant et après un tamponnement cardiaque expérimental réalisé sur des chiens à thorax ouvert. Pendant les périodes de contrôle et de convalescence, les pressions transmurales furent positives dans les deux ventricules. Pendant le tamponnement les pressions transmurales diastoliques devinrent négatives dans les deux ventricules.

Dans un groupe de chiens opérés à thorax fermé, les pressions transmurales subatmosphériques furent mesurées pendant un tamponnement cardiaque, à partir des deux oreillettes et des deux ventricules. Au cours d'un tamponnement important, les pressions intrapéricardiaques surpassèrent la pression systolique ventriculaire droite, et dans un très important tamponnement, même la pression transmurale systolique ventriculaire gauche fut négative.

Dans les tracés pratiqués pendant la surveillance et la convalescence, l'inspiration fut accompagnée d'une augmentation de la pression du pouls pulmonaire artériel, et d'une diminution simultanée de la pression du pouls aortique. Ce phénomène fut exagéré pendant le tamponnement cardiaque. L'auteur discute les conséquences de cette constatation en ce qui concerne la génèse du pouls paradoxal.

ZUSAMMENFASSUNG

An Hunden mit eröffneter Brusthöhle wurden transmurale Druckwerte beider Ventrikel ermittelt undzwar vor, während und nach experimenteller Herztamponade. Während der Zeitspanne der Kontrolle und der Erholung waren die transmuralen Druckwerte positiv in beiden Herzkammern. Während der Tamponade wurden die transmuralen diastolischen Druckwerte beider Kammern negativ.

In einer Reihe von Hunden mit geschlossenem Brustkorb wurden die subatmosphärischen transmuralen Druckwerte beider Vorhöfe und beider Kammern bestimmt während der Herztamponade. In Fällen starker Tamponade überschritten die intraperikaradialen Druckwerte den systolischen Druck der rechten Kammer; bei sehr starker Tamponade war sogar der transmurale systolische Druckwert des linken Ventrikels negativ.

Bei den Kurven während der Kontrollen und der Erholung waren die Inspirationen verbunden mit einem Anstieg des pulmonalen arteriellen Pulsdruckes und einer simultanen Abnahme des Aorten pulsdruckes. Dieses Phänomen war während der Herztamponade noch besonders stark ausgeprägt. Besprechung der sich aus diesem Befund ergebenden Folgerungen hinsichtlich der Genese des pulsus paradoxus.

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A TEST FOR EVALUATING THE PROTECTIVE POWER OF ISONIAZID

Pasquier and Mauro have studied and determined the protective power of isoniazid using C_{14} labelled tubercle bacilli. After previous treatment with the drug, mice were experimentally infected by intravenous injections with massive doses of tubercle bacilli, strain H37RV, labelled with C_{14}. Tissue radioactivity, due to bacterial diffusion, as measured with a Geiger-Muller apparatus, was found in treated mice to be 41 per cent less than in control animals.

Pasquier, J., and Mauro, B.: "Test di Valutazione del Potere Protettivo Dell'Isoniazide Mediante O'Uso di Bacilli Tubercolari ceppo H37RV Marcati con C_{14}." *Ann. Ist. Carlo Forlanini*, 20:105, 1960.

SUPRAVALVULAR AORTIC STENOSIS

Supravalvular aortic stenosis is encountered rarely. Three patients who had this condition have been operated upon with relief of the stenosis and survival of the patients. The stenotic supravalvular ring was first divided and then permanently enlarged by the suturing of an appropriate diamond-shaped prosthesis in the aortic incision. Whole-body perfusion was employed to provide the conditions necessary for the performance of the procedure. The diagnosis of this condition can be made by the technique of retrograde arteriocatheterization.

McGoon, D. C., Mankin, H. T., Vlad, P., and Kirklin, J. W.: "The Surgical Treatment of Supravalvular Aortic Stenosis," *J. Thor. Cardiov. Surg.*, 41:125, 1961.

Broad Spectrum Rehabilitation*

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Cardiovascular rehabilitation is a many-faceted tool in the hands of the physician. Its usefulness lies throughout the course of cardiovascular disease.

A rehabilitated cardiac patient may be defined as:

1. One who, within the physical limitation of his disease, has been oriented psychologically to accept the limitations and who has returned to a productive and gainful status in his community with these limitations, without fear or anxiety, and with a sense of usefulness in his own eyes and those of his associates, both at work and in the community;[1] or more concisely—

2. The art and science of restoring a person to that level of physical and mental capacity which is compatible with the functional capacity of his heart.[2]

3. Dr. William Dock[3] expressed it as restoration to an active life with avoidance of neurotic action to organic disease.

Medical rehabilitation has four major objectives, namely:

1. The *prevention* of unnecessary physical, intellectual and emotional damage.

2. The *maximum restoration* of the patient's physical ability beyond the specific treatment of the disease.

3. The attainment of the *optimal total functional status* which the patient is capable.

4. As a correlary, the *appropriate modification of the patient's environment* in order to meet his specific needs.

Rehabilitation should commence from the moment the diagnosis of cardiovascular disease is made, whether it be acute or chronic, and should continue without abatement throughout the course of the disease.

Of greatest importance is education of the patient and his family by the physician, accompanied by the maximal utilization of all the community resources, both in the acute as well as the convalescent and rehabilitative stages.

The physician today is expected not only to be well informed about medical facts, but also to be a psychiatrist, sociologist, vocational counsellor, and work physiologist. In about 80 per cent of patients, the private physician can manage the total rehabilitation. The other patients need the benefit of other disciplines and a cooridnated team approach.[4]

The primary responsibility for the total care of the patient is the physician's. The patient must not be "turned over" to those in related fields, *i.e.*, therapists of various types. Unquestionably the advantages to be gained by the team effort of various disciples: *e.g.*, a. medical, b. psychiatric, c. psychologic, d. social service, e. vocational counselling, f. occupational therapy, g. physiotherapy, should be taken advantage of.

*Presented at the 26th Annual Meeting, American College of Chest Physicians, Miami Beach, June 8-12, 1960.

There must be one person (the physician) responsible to coordinate the group effort to obtain maximal benefits. In short, the physician's responsibility for the comprehensive management of the patient inincludes: 1. diagnosis, 2. medical and/or surgical care, 3. convalescence, 4. rehabilitation and 5. the work prescription.

There are few counties where all of the community's resources have been brought together under one cover in the form of a directory for the senior citizen and the chronically ill. The Nassau County Medical Society of New York State in order to meet this need has undertaken the responsibility to assemble and publish this material. In addition, it offers a program giving special medical aid to the chronically ill and the older age group, at a reduced cost, in accordance with the policy of the American Medical Association, that is, reduce the cost of all forms of medical services to those on fixed incomes (pensioners) and those with unusually heavy recurrent expenses out of proportion to their resources (chronically ill). Early in the work of preparing this directory, it was learned that other groups in the field of health were eager to assist in this project. These included dentists, pharmacists, podiatrists, nurses, opticians, laboratories, and hospitals. They also voluntarily agreed to reduce their fees, proportionate to the needs of the patient, but still offer the same quality of care, service and interest. The Nassau County Department of Health, realizing that this directory would serve a useful public service, purchased a large quantity for distribution to the citizenry at large who could obtain it on request. In this way, the public has access to com-

TABLE 1—TABLE OF CONTENTS

PART I—Listing of Agencies under Group Headings

1. Counseling Services
2. Dental Services
3. Equipment Sources
4. Dietary Services
5. Education
6. Employment Services
7. Financial Assistance
8. Home Care and Housekeeper Services
9. Hospital Services
10. Laboratory Services
11. Legal Services
12. Medical Services
13. Mental Health Services
14. Nursing Home, Domicile, and Housing Services
15. Nursing Services
16. Optical Services
17. Pharmaceutical Services
18. Podiatry Services
19. Recreational Services
20. Rehabilitation Services

PART II—Child Care Facilities

1. For chronically ill child
2. For the well child of the chronically ill parent

PART III—Listing of Agencies caring for specific chronic diseases

1. Alcoholism
2. Arthritis and Rheumatism
3. Blindness
4. Cancer
5. Cerebral Palsy
6. Deafness
7. Defects of Central Nervous System (Spina Bifida) (Hydrocephalus) (Encephalocele)
8. Epilepsy
9. Heart Disease
10. Ileostomy
11. Kidney Disease
12. Multiple Sclerosis
13. Muscular Dystrophy
14. Poliomyelitis
15. Speech Defects
16. Tuberculosis

PART IV—Index

munity resources at all levels of illness, from the acute stage through to the rehabilitative stage.

At this point, I would like to demonstrate the table of contents of the directory (Table 1). Part one contains a list of all the agencies available to the public under various headings and includes under each agency the address, telephone, area covered, referral method, services provided, and fees if any. Part two contains a listing of the various organizations offering child care facilities. Part three contains a listing of the various organizations offering facilities for individual chronic diseases. All three sections are cross-indexed.

It is hoped that other county medical societies will exercise their leadership by offering similar services in their communities. Copies of the Nassau County Directory may be obtained by addressing your requests to The Nassau County Medical Society.

Since the establishment of the first Work Evaluation Unit in 1941, there are now about 53 units sponsored and supported by the local heart associations throughout the country. A Work Evaluation Units is composed of a staff trained in the rehabilitation of the cardiac. The staff consists of a cardiologist, vocational consultant, medical social worker, psychiatrist or psychologist, and a medical director who acts as coordinator. The team technique permits a holistic approach for examination in depth of a patient and at the same time is an invaluable research tool. In addition, it enables the private physician to obtain consultation in difficult cases, and where division of responsibility may be desired. The work unit has no fee and does not treat the patient at any time. The work unit enables the cardiac to make a successful work adjustment by:

1. Accurate assessment of his work capacity.
2. Analysis of specific jobs in terms of physical and emotional energy requirements.
3. Knowledge of rehabilitation and placement services in the community.
4. Discussion and liaison with industry and management.

Cardiacs can and do work. This is exemplified by:

a. Seventy per cent of cardiovascular patients fall into New York Heart Association Classification I and II.
b. Statistics have shown that 85 per cent of patients with coronary insufficiency can continue in employment.[5]
c. Approximately 60 per cent of individuals with myocardial infarction can return to work with little or no modification of job assignment.[6]
d. Continued employment does not adversely affect the prognosis of arteriosclerotic and hypertensive heart disease.[7]
e. About 55 per cent of individuals with congestive heart failure are employable, if individualized work restrictions are imposed.[8]
f. Many cardiacs who have undergone cardiac surgery for congenital or rheumatic heart disease can be completely rehabilitated in full time employment.
g. Recurrent attacks of rheumatic carditis are no longer a problem in medicine today and the rheumatic can look forward to a long working life.[9]

Holman[10] in an eight-year survey of a Work Classification Unit indicated:

1. Coronary heart disease is not accelerated by working. Death is usually due to a secondary myocardial infarct and not congestive heart failure.
2. Rheumatic heart disease is essentially unchanged by work. The patients fail in congestive heart failure, but late in the disease. Chemical prophylaxis should be continued 20 years after the initial attack. The last illness will be brief and the exit sudden both in aortic and mitral disease. The size of the heart is important in rheumatic heart disease, but not in arteriosclerotic heart disease, as far as prognosis to work is concerned.
3. In arteriosclerotic heart disease, the return to work stimulates longevity as compared to those at rest.
4. Valvulotomy is done only in the presence of definitive symptoms.
5. Post-operative causalgia and neuralgia are frequent, but they do stop in those with adequate motivation, in time.
6. The anxiety state is the hallmark of coronary artery disease. In 40 to 60 per cent of patients, emotional factors were next in importance to the heart disease *per se*.

The physician today must be aware of ergonomics and ergonometry, *i.e.*, processes for dealing with the measurement of the energy requirements of activity of human beings. The energy cost of such basal activity as sitting or lying is approximately 1.25 calories/min. More than 50 per cent of patients with myocardial infarction improve enough physically within three months to be able to expend 2 to 5 calories/min. in steady state exercise and 6 to 8 calories/min. in peak effort. This is well above the average energy expenditure in most occupations.[11] It is a truism that most cardiacs prefer to work than to stay at home since domestic duties require 3 to 5 calories/min. while modern factory work requires 2 to 3 calories/min. Even foundry work at 4 to 6 calories/min. is within the capacity of the patient with coronary disease who is not acutely ill or severely decompensated.

I would like to demonstrate the energy costs of some activities and occupations:[12]

TABLE 2

Activity	Cal./min.	Activity	Cal./min.
Washing and dressing	2.6	Inspector	1.2
Washing face and combing hair	2.5	Printer	2.0
Sitting or lying down	1.6	Shoe Repairer	3.0
Standing	2.0	Shoveling	10.0
Sewing, 30 stitches/min.	1.1	Postman	10.0
Peeling Potatoes	2.4	Planing hardwood	9.0
Polishing floor	4.5	Grass cutting	4.3
Bed making	5.4	Gardening	4.4-5.6
Beating and brushing carpets	7.8	Hoeing	4.4
Climbing stairs	6.0-10.0	Driving a car	2.8
Walking 3 mi/hr.	5.6	Golfing	5.0
Typing	1.5	Dancing	5.2
Tennis	7.1	Cycling	5.0-10.0

Keeping the prior chart in mind, I draw your attention to the next chart showing the inter-relationships between cardiac function classification, physiologic symptoms, and ergometrics.[13]

TABLE 3

Cardiac Functional Classification	Physiologic Symptoms	Maximum Calories/Min. sustained	Maximum Calories/Min. intermittent
I	Patients with a cardiac disorder *without limitation of physical activity*. Ordinary activity causes no discomfort.	5.0	6.6
II	Patients with a cardiac disorder with *slight to moderate limitation of physical activity*. Ordinary physical activities caused discomfort.	2.5	4.0
III	Patients with a cardiac disorder with *moderate to great limitation of physical activity*. Less than ordinary physical activity causes discomfort.	2.0	2.7
IV	Patients with a cardiac disorder *unable to carry on any physical activity* without discomfort.	1.5	

Now, I would like to call to your attention a new concept for the "work prescription." The following chart will demarcate in exactitude what each classification in the New York Heart Association's guide should be able to do. In this manner the work prescription will include: the walking, stair climbing, lifting and standing abilities. This is far more meaningful to a vocational counsellor or a personnel officer.

TABLE 4—FORMULA FOR JOB PRESCRIPTION
(Most commonly used)

	Class I	Class II	Class III	Class IV
A	WALK—unlimited STAIRS—unlimited LIFTING—60-100 lbs. STANDING—unlimited			
B	WALK—unlimited STAIRS—4 flights LIFTING—40-60 lbs. STANDING—unlimited	WALK—one mile STAIRS—1 flight LIFTING—25 lbs. STANDING—unlimited		
C		WALK—½ mile STAIRS—1 flight LIFTING—15-20 lbs.	WALK—3-5 blocks STAIRS—1 flight LIFTING—10-15 lbs.	WALK—less than 1 block STAIRS—less than 1 flight LIFTING—5 lbs. STANDING—limited, 25 per cent of time (Sheltered Workshop)
D			WALK—1-2 blocks STAIRS—less than 1 flight LIFTING—5-10 lbs. STANDING—limited, 50 per cent of time	UNEMPLOYABLE
E	U N E M P L O Y A B L E			

(Subcommittee on Cardiovascular Disease in Industry [Brooklyn Division], New York Heart Association, S. C. Franco, M.D., Chairman.)

The next chart will show the standard physical restrictions form in daily use at the Consolidated Edison Company of New York

TABLE 5—STANDARD PHYSICAL RESTRICTIONS FORM, CONSOLIDATED EDISON CO. OF N. Y., INC.

Physical Restrictions

Manual Labor

A—Only occasional pushing, pulling, or lifting up to 10-15 pounds.

B—Only occasional pushing, pulling, or lifting up to 40-60 lbs.

Climbing

C—No work requiring repeated or frequent stair or ladder climbing.

Driving

D—Not to operate motor vehicles.

E—No truck driving.

Location of Work

F—No continuous inside work.

G—No continuous outside work.

Safety of Others

H—No work involving the safety of others.

Elevation

I—No work above unprotected floor levels or about open excavations.

Live Equipment

J—No work around unprotected equipment carrying electricity, steam, or exposed moving parts.

Hours of Work

K—Work only between the hours of 6 A.M. and midnight.

L—No overtime exceeding two hours per day, six days per week.

Atmosphere

M—No coal, coke or ash handling, or work in similar sustained dusty atmospheres.

N—No work in predominantly wet or damp locations.

Temperature

O—No work in constantly changing temperatures.

P—No prolonged work in sustained temperatures below 40°.

Q—No work in artificially produced sustained temperatures above 100°.

Positions

R—No work requiring repeated stooping.

S—No work in crawling, kneeling or cramped positions.

T—No continuous walking or standing and not to exceed 50% of total working hours.

U—No work requiring talking for long periods.

Eyesight and Hearing

V—No work under conditions involving marked frequent light changes (going from light to dark or vice versa).

W—No work requiring acute (normal average) vision.

X—No work requiring normal hearing (ability to hear ordinary spoken voice).

Y—Work requiring only the use of one arm or hand.

Z—Special restriction—not covered by the foregoing—to be written out.

(Courtesy Dr. S. C. Franco, Exec. Med. Dir.)

Industry is apparently not aware of the ease and success attained in rehabilitating the large reservoir of potential workers who have mild cardiac conditions. It is estimated that in this country (U.S.A.) as a whole, 700,000 people with cardiac disease are added yearly[14] to the approximately ten million already existing.[15]

The stresses of traveling to and from a job, and the work load imposed by walking to the locker room or place of employment (average 4 to 6 calories/min.) may far exceed the expenditure of energy required to perform the job (2 to 3 calories/min. in factory work). This point brings to light the truth of the "Work Dictum" of Abilities, Inc. This is an organization, composed solely of *severely disabled* persons, who obtain contracts in open competition, pay better than average wages in the same industry, have a lower workman compensation insurance rating because of low injury rate, and a lower absentee rate than in private

industry. Their only preemployment requirement is that the individual be able to get to and from work on his own. After the employee has been working for several months does he get his physical examination. The reason for this incongruous technique is to prevent bias from a medical report to color motivation and ability. By ability, I mean what can be disclosed even with people who have not worked in years due to hospitalization and require complete training. The Governor of the State of Florida has, after a recent visit to the organization in New York, been so impressed that one is being established in his state with the major concept of putting the senior citizen to productive use.

The next chart will demonstrate the Work Prescription Form in daily use at The Consolidated Edison Company of New York.

TABLE 6—WORK PRESCRIPTION FORM

Cardiac Diagnosis:	Etiological Anatomical Physiological		
Functional Capacity and Therapeutic Classification:			
Cardiac Limiting Factors:	Limited (L) Prohibited (P)	Working Conditions:	Limited (L) Prohibited (P)
Walk		Outside	
Climb		High Temp.	
Crawl, Kneel		Low Temp.	
Stand		Sudden Temp. Changes	
Stoop, Crouch, Bend		Humid	
Lift, Carry		Wet	
Throw		Moving Objects	
Push, Pull		Cramped Quarters	
High Rate of Working Speed		High Places	
		Night Shift	

(Courtesy Dr. S. C. Franco, Exec. Med. Dir.)

SUMMARY

A tri-focal attack on rehabilitation has been discussed, viz: 1. A directory of community services; 2. work evaluation unit and a new formula for the work prescription; 3. proof that the cardiac can work as well as the non-cardiac. Most cases of rehabilitation can be managed by the private physician. One can avoid the development of iatrogenic disease by education of the patient and family and an optimistic outlook by the physician.

RESUMEN

El ataque trifocal en rehabilitación es motivo de esta disertación, o sea por: 1. un directorio de los servicios de la comunidad; 2. valuación de la unidad de trabajo y nueva formula para la prescripción del trabajo; 3. prueba de que el cardiaco puede trabajar tan bien como el no cardiaco.

La mayoria de los casos de rehabilitación pueden ser atendidos por el médico particular. Puede evitarse el desarrollo de enfermedad iatrogénica por la educación del enfermo y de la familia y por una perspectiva optimista por parte del médico.

RESUMÉ

L'auteur discute trois éléments de critiques contre la réadaptation: 1. l'annuaire des services collectifs; 2. le service pour l'estimation professionnelle et une nouvelle formule pour la reprise du travail; 3. la preuve que les cardiaques peuvent travailler aussi bien que les non-cardiaques. La plupart des cas de réadaptation peuvent être entrepris par le particien privé. On peut éviter le développement de la maladie par l'éducation du malade et de la famille et une surveillance optimiste par le médecin.

ZUSAMMENFASSUNG

Diskussion eines dreigleisigen Weges zur Rehabilitation: 1. Anweisung für die Städtischen Dienststellen; 2. Arbeitsplatzbestimmung und neue Formulierungen für die Arbeitsaufnahme; 3. Nachweis, daß der Herzbeschädigte ebenso arbeiten kann, wie der nicht Herzbeschädigte. Die meisten Fälle von Rehabilitation können durch den Hausarzt betreut werden. Man kann die Entwicklung einer iatrogenen Erkrankung vermeiden durch Erziehung des Patienten und seiner Familie und durch eine optimistische Auffassung des Arztes.

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Physical Working Capacity: An Index of Cardiac Fitness*

In 1947, T. Sjöstrand, a Swedish clinical physiologist, reported on the use of an exercise test to evaluate physical working capacity.[1] This involved performance of known amounts of work on a bicycle ergometer, with measurements of heart rate, respiratory rate and certain other responses. The estimated amount of work that would produce a heart rate of 170 beats per minute was considered the working capacity for an individual. In the normal subject, there is a linear relationship between the amount of work performed, oxygen consumption, cardiac output and pulse rate.[2] Initially designed to survey industrial problems in mine workers,[1] tests were later done to predict performance in military personnel[3] and to study the "ideal" response in trained athletes.[4]

Recently, studies[5] have been performed on 243 normal California school children 6 to 14 years old. Working capacity increased with age and body size, correlating best with surface area. Boys possessed significantly greater working capacities than girls, even at the smaller surface areas. Differences increased in the older and larger boys as contrasted with girls of the same age or size.

Similar studies[6] were performed on two groups of normal Swedish school children, 102 city and 94 country children, 10 to 12 years old. The same trends were found as in the California study with no significant difference in working capacity between the city and country groups. Likewise, no difference was found in the working capacity of California and Swedish children of the same body size. These findings are in contrast to those of others who found performance of American youth inferior to European children in certain other types of "fitness" tests.[7]

The objective evaluation of working capacity has proved valuable in studying the physiology of exercise and has permitted comparison of different groups[5,6] or the same group under different conditions.[8]

We have used this method to differentiate true vs. imagined disability in children with cardiac disease, suspected cardiac disease and no heart disease. Presently, test results in cardiac patients are compared with the data obtained on normal children, according to the percentiles for surface area. Individual patients are followed longitudinally to determine progression or regression of cardiac disability and to evaluate the effectiveness of therapy. In selected patients, it is hoped that this objective test will prove to be a valuable addition to the information obtained by history and routine examination.

*Supported in part by Grant No. RG-5735 from Unted States Public Health Service and the Association for aid to Crippled Children.

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REVASCULARIZATION OF THE HEART

The present experimental study carried out on 27 dogs demonstrated that revascularization of the heart might be performed effectively by means of fixing to it a subcutaneous pedicle. Due to profuse vascularization, ability to give origin to new vessels, plasticity, absence of degenerative changes, simplicity of the pedicle formation and minimal trauma to the body, the subcutaneous pedicle has outright advantages in comparison with other tissues suggested for heart revascularization (muscle, omentum, lung, pericardium). The study has demonstrated that in certain conditions, the pedicle vessels growing through the myocardium create a great number of anastomoses with coronary arteries and prevent destructive processes in the myocardium that are caused by the ligation of coronary arteries. The suggested method of surgical treatment of chronic coronary insufficiency is strongly recommended for clinical use.

Pofilo, P. I.: "Revascularization of the Heart (Experimental Study)," *Chest Surgery* (USSR), 85:54, 1960.

HISTIOCYTOSIS X

The authors report a case of Hand-Schüller-Christian disease in which spontaneous reversal of extensive pulmonary manifestations (infiltration and fibrosis) was noted. They refer to the observations of Hodgson *et al.* who state that the lung lesions may disappear completely or irregular linear strands of fibrosis may remain. Ponseti recorded two cases with complete disappearance of the pulmonary changes after remission. Avery and co-workers observed a series of ten cases in which the lung infiltrations resolved entirely; in one of these, the condition had persisted ten years before full resolution occurred. Evidence of interstitial fibrosis may remain for long periods and in some cases may result in cor pulmonale. The patient reported in this paper exhibited quite marked improvement in the pulmonary findings in a relatively short time.

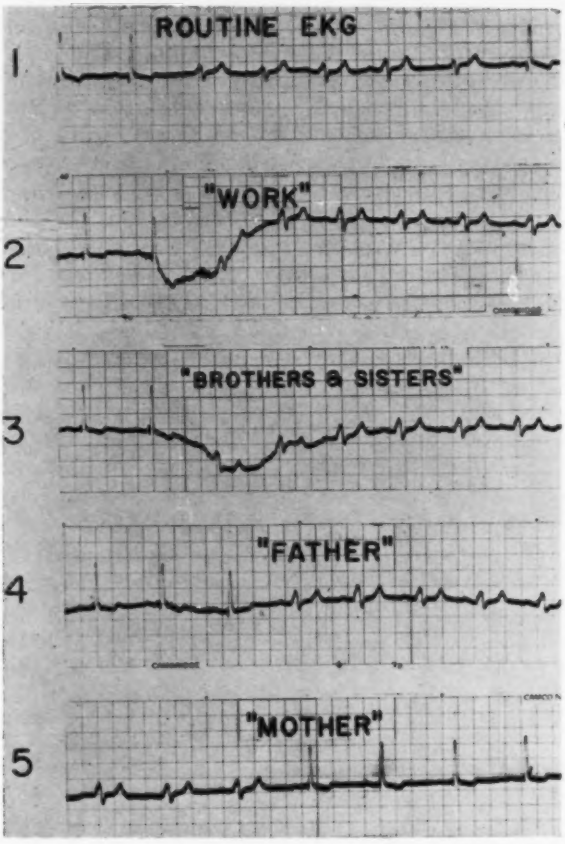
Green, A. E., and Flaherty, R. A.: "Histiocytosis X," *Radiology*, 75:572, 1960.

ELECTROCARDIOGRAM OF THE MONTH

Edited by Stephen R. Elek, M.D.

Intermittent Complete Left Bundle Branch Block Associated with Psychological Factors

The tracings are those of a 40 year-old white farmer admitted to the hospital for evaluation of acute dyspnea which became manifest on opening a silo (? Silo Filler's Disease). A routine electrocardiogram on the day of admission showed normal sinus rhythm alternating with short periods of complete LBBB (strip 1, Lead III). It was subsequently demonstrated that long runs of LBBB could be induced by administration of epinephrine and by discussion with the patient of emotionally-charged subjects. Mention of key words during a 1½-minute recording of Lead III resulted in periods of block as shown: "trouble at work" (strip 2); "brothers and sisters" (strip 3); "father" (strip 4). Interestingly enough,



mention of the word "mother" (strip 5) resulted in reversion of the LBBB pattern to normal conduction.

The phenomenon of intermittent LBBB has often been described in the literature, but its association with psychologic disturbances has been reported infrequently. Vesell in 1941 suggested that in patients with intermittent block the equilibrium between normal ventricular conduction and abnormal conduction is tenuous. Beyond a certain critical heart rate, blocked ventricular conduction occurs. This critical rate may vary between 40-200/min., and may vary in the same patient from day to day. In the present case, the block phenomenon occurred repeatedly at cardiac rates of 72-74/min., whereas normal sinus rhythm was present at lower rates.

Various effects of the autonomic nervous system have been postulated to explain transient bundle block. Both increase and decrease in vagal tone, as well as local circulatory factors and pathological anatomical changes have been implicated as etiological factors.

Follow-up tracings in our patient 18 and 22 months after the original hospital admission have demonstrated evolution of a persistent LBBB pattern despite a low cardiac rate of 56-62/min. During performance of a Valsalva maneuver, however, normally-conducted complexes were observed at a rate of 48-51/min. Following administration of 0.6 mg. atropine sulfate subcutaneously, the LBBB pattern was also converted to normal. Since the effect of such a small dose of atropine cannot be stated definitely, it is uncertain whether the attendant return of normal conduction was secondary to an increase in vagal tone or a vagolytic action, although the former is suggested. (Since this small dose of atropine would be expected to produce vagal stimulation rather than vagolytic action, the attendant return of normal conduction with a decreased heart rate would suggest that an increase in vagal tone is not the basis of the abnormal bundle branch conduction in the present case.)

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The Committee on Electrocardiography and Vectorcardiography welcomes comments. We would also be pleased to receive EKG's of exceptional interest with brief history. Please submit material to: Stephen R. Elek, M.D., chairman, 6423 Wilshire Boulevard, Los Angeles 48, California.

Editorial

Permanent Tracheostomy for Pulmonary Cripples

The management of pulmonary cripples today is one of the most serious challenges encountered by chest physicians. The number of these patients has been increasing steadily since modern chemotherapy and chest surgery have so effectively prolonged the lives of those who would otherwise have died of tuberculosis, of bronchopulmonary suppurative disease, of bronchial infections in emphysema, and even of lung cancer.

About 10 years ago, we had occasion to treat several patients with pulmonary disease who had had emergency tracheostomy performed for relief of laryngeal obstruction long before they had developed into pulmonary cripples. As lung function deteriorated and these patients began to suffer from increasing dyspnea, we were able to alleviate them markedly by preventing airway obstruction through catheter suctioning. Two such patients with extreme pulmonary insufficiency amazed us by their survival in relative comfort for many years by means of frequent deep suctioning. We then believed that this might prove a new useful tool in the management of pulmonary cripples. However, some time later, we became aware of the fact that for nearly a decade tracheostomy increasingly had been resorted to in all types of respiratory emergencies.

Today, tracheostomy is one of the most common surgical procedures performed upon both medical and surgical patients. Every medical center of some size now has a so-called "respiratory unit" organized for respiratory emergencies, resuscitating patients in respiratory failure and prolonging life in those with respiratory insufficiency. The medical and surgical conditions in which such difficulties arise are constantly expanding. There is an enlarging number of patients requiring emergency treatment and specialized after-care in these "respiratory units." This involves the use of mechanical respirators usually by way of tracheal cannula with adapter; and so, tracheostomy, cannulization and catheterization of the trachea have become the most essential part of the service of these teams. Today, an increased proportion of emergency cases treated by these "respiratory units" are patients with chronic pulmonary disease suffering acute attacks of pulmonary insufficiency.

By now, tracheostomy has been performed upon many pulmonary cripples during acute emergencies with at least temporary life-saving effect. Confirmation of this has come to us in numerous communications we have had with many medical and surgical centers in this country. During recent travels abroad, we were also able to confirm this in conferences with physicians and surgeons on the continent. In England, where chronic lung disease is so widespread and the number of pulmonary cripples is exceptionally large, emergency tracheostomies have for a number of years been frequently performed. In a recent special symposium of the British Royal College, tracheostomy for such purposes was made the subject of broad discussion.

Accordingly, a few years ago, we proposed elective tracheostomy as a measure in treatment of progressive pulmonary insufficiency, citing the possible advantages of such in the prevention of acute episodes. The difficulties and risks of emergency tracheostomy in patients with acute pulmonary insufficiency are well recognized. Experience of the past few years has convinced us that the goal should be an elective operation resulting in a firm mucocutaneous opening* that can remain permanent if necessary. This goal involves medical and surgical problems which still remain to be worked out through cooperation of internist and surgeon.

The exact *indications for permanent tracheostomy* have not yet been accurately defined and therefore, one cannot be dogmatic in regard to its use. In light of our own experience, as well as that of others with whom we have been privileged to collaborate, we consider the following conditions those in which this procedure is well worth a trial:

1) the patient with chronic *far advanced obstructive emphysema* who is having *recurrent bouts of acute pulmonary insufficiency* which are frequently brought on by a trivial infection, or overexertion or a mild bout of congestion; during these attacks, signs of progressive hypoventilation and cough failure sooner or later develop. Here an ensuing vicious cycle may rapidly prove fatal unless timely ventilation and airway clearance is provided by mechanical means. Tracheostomy here is to be an elective measure done prior to the onset of severely depressed breathing;

2) patients who become *pulmonary cripples following pneumonectomy or thoracoplasty*. Usually these patients live comfortably for many years, until finally the remaining lung becomes emphysematous leading to great loss of pulmonary reserve. Following the progressive development of severe dyspnea and exhausting cough and difficult expectoration, a number of such patients have been greatly benefited by permanent tracheostomy with catheter suctioning and have gone on to practical complete rehabilitation;

3) patients with advancing insufficiency having a *persistent ineffective cough* eventuating in *syncope and blackouts*. Several such patients whom we were privileged to observe** have now been free of any such further blackouts for two years after permanent tracheostomy (termed "tracheal vent").

Apropos of the latter, its mechanism is of particular interest in shedding light upon the possible effect of tracheostomy in emphysema. The act of coughing is generally described as a forcible expiratory effort against a closed glottis. When the air pressure in the chest reaches a high level, the glottis suddenly opens and air under pressure is expelled with great force and velocity, carrying with it the mucus in its path. Recent roentgen kymographic studies (Weber) have revealed that "cough failure" in emphysema is due to fundamental differences from coughing in normals. In normal lungs great volume changes occur during coughing, but there is little change in the lumina of bronchi and trachea. Contrariwise, in emphysema during coughing there is little

*For a simplified technic, refer to: E. Naclerio; A. Penta.
**Operated and reported upon by Dr. E. Naclerio.

change in lung volume, but there is marked reduction in the bronchial and tracheal lumina. Massive tracheal collapse was shown to be diagnostic of emphysema and to be the explanation of cough failure. If these observations are correct, the effect of "tracheal vent" in emphysema can be based on prevention of excessive pressure and tracheal collapse during cough.

Among the *favorable effects of tracheostomy* noted are lessened dyspnea, easier cough and expectoration and relief from the distressing anxiety that is so often associated with spells of smothering incited by recurrent bouts of ineffective coughing. Temporary increase of secretions following tracheostomy and suctioning has not interfered with patients' improvement.

Increased secretion through suctioning often occurs. This in itself may even be helpful in patients with severe emphysema who not infrequently have little secretions. Normally, the lungs are quite moist organs and have a large fluid circulation, the source of which is threefold: (1) serum constantly filters out of alveolar capillaries in amounts which keep the air in the lung fully vapor-saturated. More than a pint of fluid is thus evaporated from the lungs daily; (2) a considerable amount of mucus is secreted normally by the cells lining the bronchial tree; (3) quite recently it has been found that the lining cells of the bronchiolo-alveolar junctions constantly secrete a *special type of mucolipid substance* which serves to suppress surface tension in the airspaces. Most of this *moisture keeps flowing upward* on the ciliary escalators of the airways in a constant stream. This is accepted as playing an important role in the *self-cleansing function* of the lungs. In so-called dry emphysema, this fluid stream is diminished. We have found that deep catheter suctioning often starts it up again. The clinical improvement which can occur at the same time, we have assumed to be related to the increased secretion induced by catheterization.

Clinical observations indicate that in patients with chronic pulmonary disease and copious secretions there is apt to be severe bronchitis and/or bronchiectasis with moderate emphysema. In our experience patients with such copious secretions benefitted little and only temporarily from tracheostomy. We were not able, even with frequent suctioning, to get ahead of the excessive secretions. We do not consider suppurative bronchial disease an indication for tracheostomy.

We have been able to confirm earlier observations that severe bronchitis, copious secretions and moderate emphysema are apt to lead more often and earlier to pulmonary heart disease, while severe emphysema, a form less likely to have copious secretions, leads infrequently and later to pulmonary heart disease. This is particularly true of patients with so-called vanishing lungs.

The *rationale of tracheostomy* with suctioning in the management of pulmonary cripples is still a matter of speculation. At first it appeared to us, as it still does to many observers, that it is a mere matter of "bronchial toilet." However, the relief of secretional obstruction does not alone explain its action. It is true that considerable reduction of functional as well as of anatomic deadspace occurs. In addition we often

stimulate production of secretions of a less viscid nature which is expectorated with greater ease with the cough incited by suctioning. Strong suctioning from the depths of the lungs may diminish air trapping. "Tracheal vents" may profoundly change the dynamics of coughing. The prevention of a build-up of excessive pressure in the lungs about the upper airways may remove obstruction to effective cough. Perhaps these and other undefined factors play a part in the relief of dyspnea. The problem is far more complex than is generally believed.

In summary, permanent tracheostomy with suctioning in chronic advanced pulmonary insufficiency has not been employed in a sufficiently large number of patients, nor for a long enough period of time to permit dogmatic statements. For the advanced pulmonary cripple, it is for the most part only a palliative measure which at times may be dramatic. Occasionally it has proved successful in rehabilitating a patient. The constantly repeated early post-operative suctioning can prove rather distressing to patients and this period particularly should have trained nursing personnel. Tracheostomy frequently fails of its purpose, perhaps because it is performed too late or because the indications, contraindications and mode of action are not yet accurately defined. On this basis we suggest that if it is performed, it should be explained to the patient beforehand that it is done on a temporary basis and that thereafter he may have the choice of keeping it permanent or not.

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PLAN NOW TO ATTEND THE MEETING OF THE YEAR

27th Annual Meeting, American College of Chest Physicians
Hotel Commodore, New York City — June 22-26, 1961
Joint Meeting with American Medical Association — Monday, June 26

We hope that you have already drawn a large red circle around the dates June 22-26. These are the dates of the College meeting which culminates in a combined meeting with the American Medical Association on June 26.

If you have studied the program printed in the special section of the March issue of DISEASES OF THE CHEST, you already know the splendid calibre of the scientific program in store for you. A separate copy of the program has also been mailed to you.

Here is a check list of four important steps which may help you in planning to get the most out of the meeting.

1. REGISTER IN ADVANCE
   By completing the advance registration form in the program and returning it to the Executive Offices of the College, you will avoid the necessity of standing in line at the registration desk. Your badge and program as well as luncheon, banquet, and seminar tickets will be awaiting you at the Commodore Hotel.
2. SELECT ROUND TABLE LUNCHEONS
   Round table luncheon discussions will be held on Friday, Saturday and Sunday, June 23, 24 and 25 at the Commodore Hotel and on Monday, June 26, at the Park Sheraton Hotel. The Monday luncheon is a joint presentation of the College and the American Medical Association. The subjects and speakers are listed in the program. Tickets for many of these luncheons are usually sold out in advance of the meeting and members are urged to make their reservations at once.
3. RESERVE YOUR BANQUET TICKETS
   The Annual Presidents' Banquet on Sunday evening, June 25 is the College social function of the year. Places are assigned in the order in which requests are received. Avoid disappointment by ordering your tickets now.
4. MAKE YOUR HOTEL RESERVATIONS
   If you have not already done so, now is the time to reserve hotel accommodations. Rooms will be at a premium and you will want to ensure your comfort and that of your family. A hotel reservation form is provided in the program .

You may find it helpful to look over the outline of events listed below which will serve to remind you of some of the highlights of this exceptional meeting.

OUTLINE OF EVENTS

Thursday, June 22

Postgraduate seminars

Friday, June 23

Open Forums
- Council on Undergraduate Medical Education
- Committee on Tuberculosis

Joint meeting, Board of Governors and Board of Regents

Open administrative meeting

Council and committee meetings

Round table luncheon meetings

New York State Chapter
- Howard Lilienthal Lecture

Saturday, June 24

Scientific sessions
- Cine Symposiums
  - Fibrinolytic therapy in acute coronary thrombosis
  - Thoracic surgical emergencies in infants

Round table luncheon meetings

Motion picture session

Symposium on medical aspects of air pollution

Emphysema and pulmonary physiology

Cardiovascular problems in children, including the newborn

Sunday, June 25

Scientific sessions
- Tuberculosis and other pulmonary diseases
- Tumors and pulmonary physiology
- Coronary and myocardial diseases
- Visual aids in cardiologic diagnosis
- Panel discussions
  - The new and old in the treatment of hypertension
  - What's new in cardiovascular surgery

Motion picture sessions

Round table luncheon meetings

Convocation
- Louis Mark Memorial Lecture

Cocktail party, Banquet, Dance

Monday, June 26

JOINT MEETING WITH AMA

Scientific Session (New York Coliseum)

Symposium on new approaches in treatment of acquired heart disease

Panel discussion on steroid treatment in lung disease

Symposium on modern diagnostic measures in cardiac disease

Scientific papers on pulmonary disease

Round table luncheon meetings (Park Sheraton Hotel)

Fireside Conferences (Hotel Commodore)
- 36 tables, prominent scientists discussing recent advances in cardiopulmonary diseases

Be sure to visit the special scientific exhibits on Physiologic Testing of Cardiac Function and Pulmonary Function Testing at the New York Coliseum, June 25-30.

Obituary

CHEVALIER LAWRENCE JACKSON
August 19, 1900—January 13, 1961

Chevalier L. Jackson, M.D., M.Sc., born in Pittsburgh, received his Medical Doctorate from the University of Pennsylvania in 1926. His interest in bronchoscopy developed during his postgraduate work; however, the close supervision of Chevalier Jackson and the teams of associates he had trained probably intensified his determination to prove himself in his own right. This zeal and drive characterized his very busy life. Never satisfied to accepted the position of the son of a famous father, his internationally recognized career in medicine furthered the research and clinical achievements in laryngology and bronchoesophagology developed by Chevalier Jackson.

"C. L." as he was known to most, "Chevy" to some, and "Lawrence" to a few, received the M.Sc. (med.) degree from the University of Pennsylvania in 1930 and shortly thereafter accepted an appointment in his specialty at Temple University. As the result of his own contributions he was appointed Professor and Head of the Department of Laryngology and Broncho-Esophagology at Temple in 1946. Yet his activities in teaching and organizational medicine were of such international scope that few, if any, can match the breadth of recognition he received and the friendships he made throughout the world. He was invited to give lectures and courses on every continent and was an honorary or corresponding member of most national societies of otolaryngology, bronchoesophagology and diseases of the chest of Latin America, Europe and Japan. He was a Commander of the Order of the Liberator San Martin (Argentina), a Chevalier, Legion of Honor (France) and an Honorary Member of the Faculty of Medicine of the Universities of Chile, Mexico and Uruguay. In the United States he was a distinguished member of all the national and many regional societies of otolaryngology and bronchoesophagology, including the American Laryngological Association and the American Broncho-Esophagological Association of which he was president; he was a member of the American College of Surgeons and the American Association for Thoracic Surgery.

Dr. Jackson became a Fellow of the American College of Chest Physicians in 1935 and was its President in 1951-52. Always active in its meetings, he was chairman of the Council on Pan American Affairs for many years and chairman of the Committee on Membership at the time of his death. He was also active on the national and international committees on bronchoesophagology of the College. In addition to his many scientific contributions, these committee activities were directed toward international participation and in his extensive travels he invariably carried with him his briefcase containing a multiplicity of organizational projects. He founded and served as Secretary of the Pan American Society of Otolaryngology and Bronchoesophagology and the International Bronchoesophagological Society, was active as Director of the Pan American Medical Association, and was a founder member of the World Medical Association. His ability to converse in a number of languages was remarkable, and prior to foreign travel he invariably studied the language of the country which he was going to visit. He was extremely interested in medical photography and pioneered in endoscopic, as well as sound-correlated laryngeal photography technics.

In 1929 Dr. Jackson married Hilda B. Cowling who survives him with their daughter, Joan, her husband, Frank Bugbee, and their two children, Frank and Susan.

"C. L.'s" love of music, and opera particularly, was expressed with the same intensity that characterized his medical life. In his own community he took pride in his position as President of the Philadelphia Grand Opera Company. For this and for his internationally recognized medical skills, he was held in high esteem and honor by the citizens of Philadelphia, as well as by his medical colleagues throughout the world.

PAUL H. HOLINGER, M.D.